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The Journal of Allergy

VOL. II JULY, 1931 No. 5

Original Articles

STUDIES IN CONTACT DERMATITIS

I. THE NATURE AND ETIOLOGY OF POLLEN DERMATITIS*

AARON BROWN, M.D., E. L. MILFORD, M.D., AND A. F. COCA, M.D.
NEW YORK, N. Y.

IN RECENT years, much consideration has been given to the etiology of allergic dermatoses. The experimental work has proceeded toward two objectives, one of which was to show that the cutaneous sensitiveness in human beings to primrose and poison ivy can be experimentally induced (Low,[5] Bloch,[2] H. W. Straus[9]), while the other was to prove that the specific dermatitis to nonantigens, such as nickel and arsenical compounds, which are often encountered in human beings, can also be induced in lower animals (Walthard,[14] W. Frei,[3] Sulzberger and Wise[10]).

Both of these lines of investigation have been thought to have a bearing upon the question of the influence of heredity in the etiology of human allergic disease. Bloch has reported 100 per cent success in the experimental establishment of primrose sensitiveness in human beings, and Doerr looks upon this result as contradicting the assumption of a controlling atopic hereditary influence, which has been defended by one of us. Doerr maintains that the different forms of human allergy represent merely quantitatively different expressions of the same phenomenon, which is always produced by the same mechanism, and he bases this view largely on Bloch's success in the experimental sensitization of human subjects with the active substance of primrose, believing that the establishment of any hypersensitiveness in the human being depends upon a suitable contact with the excitant together with a certain predisposition, which is possessed in merely quantitatively different degree, by all persons. But Bloch was study-

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Read before the Seventh Annual Meeting of the Society for the Study of Asthma and Allied Conditions, Atlantic City, N. J., May 2, 1931.

ing contact dermatitis (also called dermatitis venenata), a condition which is evidently not subject to the atopic influence and which represents a hypersensitiveness to nonantigenic excitants.

In recent years, cases have been reported that seemed to bridge the interval which had been supposed to exist between the inherited hay fever and the noninherited contact dermatitis. These are the instances of seasonal dermatitis in hay fever subjects which has been shown to be due to pollens.

The first experimental observation of pollen dermatitis was made by Blackley[1] in 1874. He reported the occurrence of a dermatitis of the scalp and face by wearing his hat containing rye *(Secale cereale)* in full bloom.

Walker[13] in 1918 wrote: "The protein of horse epithelium, ragweed and timothy pollen may cause eczema both from external and internal injection in predisposed persons."

Sutton[11] in 1919 has observed and reported a peculiar type of dermatitis in a farm laborer due to the pollen of ragweed. He considered it as an anaphylactic phenomenon. It is interesting to note that in discussing this view Simpson[8] opposed it and suggested that the dermatitis might not have been a reaction to the pollen protein but to alcohol-soluble nonprotein constituents as is the case with ivy dermatitis.

Thommen[12] recently reported a case of severe ragweed dermatitis developing on the arm at the injected area. He also attributed the rash to the pollen excitant.

Sulzberger and Wise[10] in a study of a case of ragweed dermatitis found that tests performed with the usual scarification method were negative, whereas contact tests yielded positive reactions. On the basis of this observation these experimenters advocated the use also of the contact method in testing for general hypersensitiveness. In the opinion of these authors the ragweed pollen allergen was the cause of the dermatitis.

As evidenced from this brief review of the literature, all the investigators of this problem have attributed the lesions to the pollen atopen. None of them suspected the possibility of the operation of a different mechanism.

Milford[6] points out in his paper that a definite reaction can be elicited in ragweed-sensitive individuals with the oily residue obtained from an extract of the pollen made with the usual fat solvents. He also states that tests with the oil occasioned in a few cases a severe dermatitis after an incubation period ranging from one to five weeks.

In regard to the immediate specific reactions just mentioned, the assumption of mere contamination of the oil with the extremely active

pollen atopen, the latter being to some extent soluble in the oil, seems the only logical one. Of much greater importance from both an etiologic and a therapeutic standpoint is the second observation, that is, the late dermatitis.

The primary purpose of this study is to *establish an etiologic relationship between pollen dermatitis and pollen oil,* in other words, *to prove that the pollen oil and not the pollen atopic excitant is the cause of the dermatitis.* This idea was strongly supported by the preliminary examination of Case 1 and Case 2 which we are about to describe, and it was proved to be correct by the subsequent experimental studies.

CASE REPORTS

CASE 1.—The patient, W. M., aged 52 years, was referred to the Bellevue Hospital Medical College, Dermatological Allergy Clinic in August, 1930. He gave a history of attacks of an intensely itching general eruption which began in spring and continued till fall. When the condition first appeared, twelve years before, the patient was living on a farm in central Virginia. During the six years of his stay in Virginia the eruptions appeared regularly in May and continued throughout the summer. He had a remission in the fifth and sixth years in late July and early August, when he visited Philadelphia for these periods. The eruptions reappeared with full intensity when he returned to Virginia. For the past six years he has been living at San Clemente, California. His rash, in this locality, was as severe as usual and ran about the same course. His symptoms improved when he went to the mountains and returned when he came home. During all this time he never had any symptoms of seasonal hay fever or asthma. His father had late hay fever. When first seen on September 4, 1930, W. M. showed an eruption distributed generally over the body, but more pronounced on the face and arms.

Routine intradermal tests with proteins gave negative reactions. Test with a strong aqueous extract of ragweed pollen (0.1 mg. N. per cubic centimeter) gave a lumpy sort of reaction without erythema, very slow in its development; it was later considered to be nonspecific because not transferable passively (Prausnitz-Küstner technic). Tested with ragweed pollen oil (ethyl ether extract residue) with the scratch method, the patient gave no immediate reaction. On patch test with the same oil he developed, after six days, a severe local rash with a definite eczematous area, similar to the one he showed on the arm when first seen. As a result of the test, the patient complained of an aggravation of general symptoms (the appearance of the rash on the face and body accompanied by intense itching).

CASE 2.—The patient, B. F., male, aged 38 years, suffered with late hay fever since June, 1923. His family history was negative. For the

past three years he had a severe and generalized skin eruption lasting from August 25 until frost. When first seen on September 1, 1930, he showed a severe dermatitis involving the face and the body generally with intense itching. At that time, the patient complained more of his itching eruption than of his hay fever. Upon test, a marked reaction was obtained to ragweed pollen in a dilution of 0.01 mg. N. per cubic centimeter. The patient was free from hay fever symptoms by the third of October; his eczema, however, persisted until November 7. Scratch test with ragweed pollen oil (ethyl ether extract residue) gave a marked immediate reaction. Patch test with the same preparation reproduced locally his original lesions after an incubation period of seven days. The patient complained of intense itching sensation over the entire arm on which the test was applied.

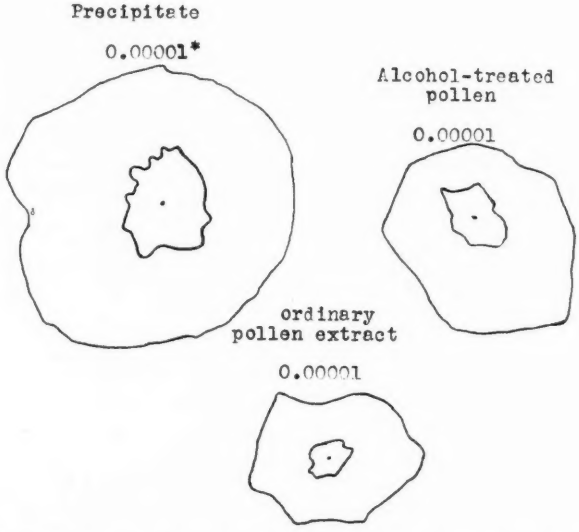

Fig. 1.—Showing the well preserved activity of the alcohol-acetone precipitate obtained from the ragweed pollen extract; tested by intracutaneous injection in a Class AA ragweed-sensitive person.

*The figures give the milligrams of nitrogen in one cubic centimeter of the extract.

It was evident that the solution of the main issue in this study hinged upon the results of comparative patch tests with the defatted pollen on the one hand and the pollen oil free from the atopic excitant on the other.

EXPERIMENTAL

The preparation of the oil-free pollen atopen was carried out as follows: high ragweed pollen collected in September, 1930, was extracted in a Soxhlet apparatus with petroleum ether until no oily residue was left upon evaporation of the final running of the solvent. The pollen was subsequently extracted in a Soxhlet apparatus with freshly distilled anhydrous ethyl alcohol. This alcoholic extraction removed a

further quantity of oil equal to about 3 per cent of the weight of the pollen. An aqueous extract of the defatted pollen was made using Coca's alkaline medium in a proportion of three grams of pollen to 100 c.c. of fluid. The extraction was carried out for fifteen minutes and the extract passed at once through a Seitz filter in order to sterilize it. This aqueous extract was precipitated with 15 volumes of a mixture of equal parts absolute ethyl alcohol and acetone. The precipitate was collected by centrifugation, dried and pulverized. On scratch test it produced a marked reaction in the least sensitive ragweed hay fever cases. It is interesting to note that the alcohol treatment did not affect the pollen atopic excitant. In fact an extract of the precipitate as well as of the ether-alcohol-treated pollen was found more active than our usual extract when diluted on the basis of the nitrogen content. This lack of correspondence between the nitrogen

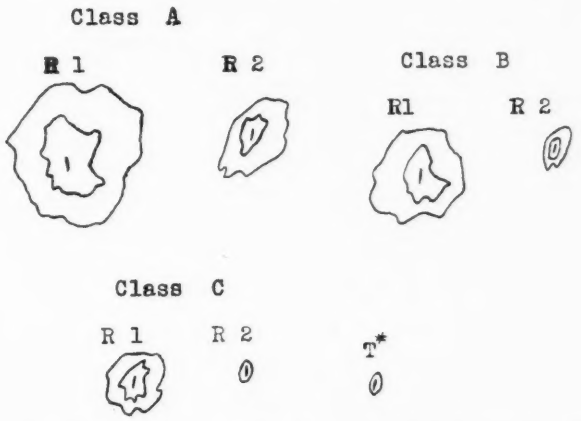

Fig. 2.—Showing the immediate reaction to a scratch test with two ragweed pollen oil preparations: R I (7 mg. of nitrogen per cubic centimeter) and R 2 (1.0 mg. of nitrogen per cubic centimeter) in the skin of three ragweed-sensitive persons.
*T = test with timothy pollen oil.

content and the activity of the pollen extract, with the least change in the technic of preparation is well known. It was proved by Grove and Coca[4] in their pollen dialysis and digestion experiment and in an unpublished experiment by E. L. Milford, who by prolonged dialysis alone was able to bring the nitrogen content of an extract from 0.3 down to 0.01 and yet found that both extracts were equal in activity when diluted on the basis of the original volume of the specimens.

With this highly active oil-free pollen precipitate we carried out a patch test upon the skin of the individual described under Case 1. The skin was scarified and the precipitate, slightly moistened, was applied to the scarified area. No immediate reaction developed (since the individual was insensitive to the pollen atopen), and after about half an hour the area was covered with a square of wax paper and adhesive plaster, which held the precipitate in contact with the skin.

After three weeks, during which dermatitis failed to develop, the patch was removed. This experiment demonstrated the inability of the atopic excitant to cause the pollen dermatitis.

In four other cases (all subjects of late hay fever) in whom the pollen oil gave a positive reaction, a patch test with the precipitate was negative after three weeks.

In preparing the ragweed pollen oil free from the atopic excitant we used as our chief criterion of the complete destruction of the atopen, the inability of the oil to produce an immediate reaction with the scratch technic in the skin of subjects of ragweed hay fever.

As a secondary indication, we made use of the nitrogen content of the oil. It will be seen in Fig. 2 that the oil preparation possessing the least power of producing the immediate reaction showed also the lowest nitrogen content.

It is a well-known fact that ethereal extracts of animal tissues contain a considerable amount of nitrogenous matter and even of antigenic proteins. Moore, Cromwell and Moore[7] have recently reported the presence of nitrogenous substances in an ether extract of pollen; they stated that 10 of 20 ragweed-sensitive hay fever subjects give positive reactions to the extracted ragweed pollen oil when tested with the scratch method; all of these, however, reacted negatively to a similar test with the oil after it had been dialyzed through a rubber membrane. These observations seem to be correct although it is not possible to repeat them, on account of the fact that these authors did not report their experiments in exact quantitative detail.

In passing, we may remark that our own present study indicates that the cutaneous reactions obtained by these authors with the pollen oil were due to the presence in the oil of contaminating hay fever excitant.

By extracting 30 grams of ragweed pollen with about 50 c.c. of ether which was not water free, and after dialyzing this extract against ethyl ether through a rubber membrane, it was found that 1 c.c. of the dialyzed oil free from ether contained one milligram of nitrogen and that, with the scratch method, the dialyzed oil was capable of producing an immediate reaction in the more sensitive ragweed hay fever subjects. Even pollen oil that had been obtained by extracting with the water-free carbon tetrachloride and had been dialyzed through rubber against this menstruum still produced an immediate reaction in the more sensitive ragweed hay fever subjects. It seems probable that Moore, Cromwell and Moore tested their dialyzed oil in less sensitive subjects.

From these experiences we came to the conclusion that these methods were not sufficient to eliminate completely the action of the atopic excitant.

However, we were able to accomplish this by shaking the pollen oil that had been extracted with CCl_4 in its solution in this menstruum with an equal volume of N/10 NaOH which quickly destroys the pollen atopen. A stronger solution of the alkali has the disadvantage of saponifying the oil.

Ragweed pollen oil treated in this way was found to have lost completely its power to produce an immediate reaction in highly sensitive hay fever subjects.

Tested with the patch method on the skin of our Cases 1 and 2, the atopen-free ragweed oil produced the typical dermatitis, a reproduction of which is shown in Fig. 3. This test was not carried out in the ragweed season, but in the month of February.

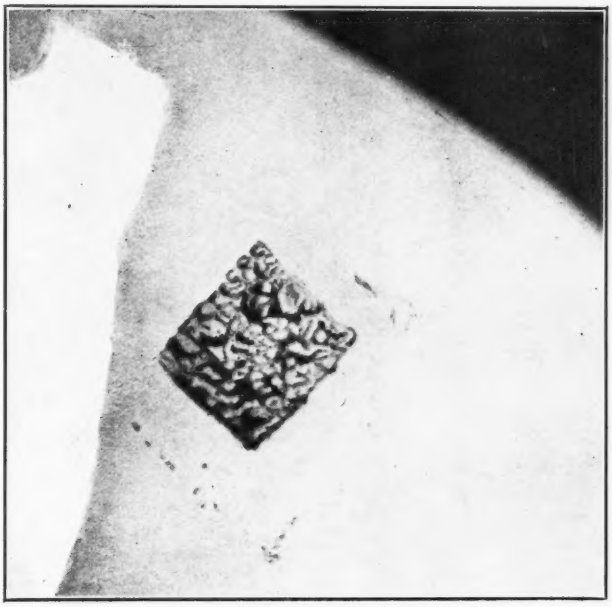

Fig. 3.

There is no further question that ragweed pollen dermatitis is produced by the oil of the pollen and not by the atopic excitant.

This preparation has been used in all of the subsequent experiments upon ragweed oil dermatitis.

The demonstration that ragweed pollen dermatitis is caused not by the antigenic atopic excitant of the pollen but by the presumably nonantigenic oil indicates that this condition belongs in the class of contact dermatitis, that is, in the same category as ivy, sumac and primrose sensitiveness.

If this assumption is correct, it must be expected that ragweed dermatitis is not confined to persons subject to the atopic hereditary influence, but occurs in equal proportion also in nonatopic persons.

We have investigated this by testing three different groups of people with the treated pollen oil: 40 individuals subject to ragweed hay fever, 40 subject to other atopic hypersensitiveness, and 40 normal persons without individual or family atopic history.

Hypersensitiveness to the oil applied with the patch technic was found in six individuals of each group. Fig. 4 shows the reaction obtained in one of the normal persons.

Fig. 4.

The results of this investigation naturally suggest a similar differentiation of the excitant of atopy and of dermatitis in other materials, and it is obvious that this principle must be important in the diagnosis and also in the treatment of dermatitis caused by materials containing atopic excitants.

The results make it clear, also, that the instances of dermatitis caused by such materials cannot be looked upon as connecting the two categories of the inherited atopic hypersensitiveness and the non-inherited contact dermatitis; the separate identity of these two categories is maintained in every essential character of the two forms (the

nature of the excitant, the character and incubation period of the reaction, and the method of its production by test).

SUMMARY

It has been thought that the dermatitis caused by pollen and experimentally reproducible by cutaneous testing with pollen oil, is due to the presence in the oil of the atopic excitant. We have been able to show that the dermatitis is not due to the atopic excitant but to the oil itself. Hypersensitiveness to the pollen oil occurs in 15 per cent of hay fever subjects, in 15 per cent of atopic persons not subject to hay fever and in 15 per cent of nonatopic persons. It is thus to be classified as a contact dermatitis similar in its nature to dermatitis due to poison ivy, sumac and primrose.

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(*For discussion, see page 398.*)

THE EFFECT OF TONSILLECTOMY IN ALLERGIC CONDITIONS*

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ROCHESTER, NEW YORK

APPROXIMATELY one-half the school population of the urban communities of the country have been subjected to tonsillectomy. This places this operation second only to vaccination for smallpox and treatment with toxin-antitoxin for diphtheria as a public health measure.

Laymen have been educated to accept tonsillectomy as a relief measure for many disease conditions, especially those presenting symptoms of obstruction to normal breathing. One cannot fail to be impressed by the frequency with which the following questions are asked by patients suffering from allergic manifestations in the nose or lungs: "Do you think I have adenoids?" or "Will it help my lungs if my tonsils are removed?" and by such statements as, "I thought my child's asthma would stop after his tonsils were removed." Rather frequently a patient states that he was told by his doctor that removal of his tonsils would cure his asthma or hay fever.

This view is not accepted by most writers on allergy. Of the material on this subject which has sufficiently solidified to reach book form, such authors as Cooke,[1] Alexander,[2] Van Leeuwen,[3] and Rackemann,[4] do not mention tonsillectomy as a method of treatment. Scheppegrell[5] thinks that enlarged tonsils which are usually associated with adenoids tend to make children more susceptible to hay fever, and that their removal is indicated not only for the hay fever, but also for their effects on the respiratory passages generally, and the ears. Walker[6] says, "Of course diseased teeth, tonsils, adenoids, and nasal spurs require removal." Thomas[7] believes that removal of tonsils and adenoids is rarely followed by relief of asthma. Balyeat[8] states that the removal of diseased tonsils may give relief from asthma for a short time in some cases.

Duke[9] compared a group of 1,000 individuals with allergic manifestations with another group of 1,000 patients presenting other medical conditions, and noted that the incidence of chronically infected tonsils in the first group was strikingly low.

In the vast periodical literature on tonsillectomy, I was able to find only a few papers dealing with tonsillectomy in allergic conditions. Peshkin,[10] in a study of 100 cases of asthma in children, concluded

*Read before the Seventh Annual Meeting of the Society for the Study of Asthma and Allied Conditions, Atlantic City, May 2, 1931.

that tonsillectomy aggravated the condition in 3 per cent, and that but one patient was improved by the operation, and then only temporarily.

Hutchison[11] believes tonsillectomy is desirable if the enlargement causes obstruction, or if the tonsils are infected, although he thinks asthma is not likely to be benefited unless it is of the "bronchitic type."

Coke[12] in a review of 1,000 cases of asthma classifies one group as having asthma with enlarged tonsils, and thinks that such patients can only be relieved by tonsillectomy.

Stout[13] in a group of asthmatic patients (number not given) states that 65 per cent of the patients whose tonsils were not removed showed moderate to marked improvement, as a result of treatment, and that 66 per cent of the patients on whom tonsillectomies were done came under the same classification. There were 12 per cent failures in both groups.

For the purpose of this paper, the records of six hundred patients have been studied. They have been seen partly in private and partly in clinic practice. All have been followed for at least one year, and many for ten years, by personal observation or by letter. All presented symptoms of the allergic type in the upper or lower respiratory tracts; many presented both nasal and lung symptoms. Patients with obvious gross infectious processes, such as chronic sinusitis, chronic bronchitis with bronchiectasis, etc., which, alone, seemed to be responsible for their symptoms, have been excluded. On three hundred of these patients tonsillectomies have been done. The remaining three hundred serve as controls. The two groups were similar as to ages when they presented themselves for treatment.

It has seemed to me proper to consider allergic coryza and allergic manifestations in the lungs, together in this study, because (a) they so frequently result from the same cause, especially in patients hypersensitive to the inhaled allergens; (b) the mechanism of production of symptoms is similar; (c) such a large number of patients present both groups of symptoms; and (d) because the question of the propriety of tonsillectomy as a remedial measure arises with equal frequency in both conditions.

Fifty-three per cent of the 600 patients were males and 47 per cent females.

Positive skin reactions were obtained, by means of the scratch test, in 79.6 per cent of the patients.

The diagnoses were listed as follows:

Asthma	429
Seasonal hay fever	230
Perennial hay fever	55
	714

In 114 patients, both the nasal and the lung symptoms were sufficiently striking to warrant classification under both headings. In many patients who suffer from asthma, the lung symptoms are so outstanding that the relatively minor nasal difficulty is not mentioned in the records. If such notations had appeared in all the records, the group under the heading, perennial hay fever, would have been much larger.

In the group of 300 subjected to tonsillectomy, and the control group of 300, the classifications were:

	Tonsillectomy	Control
Asthma	191	238
Seasonal hay fever	111	119
Perennial hay fever	40	15

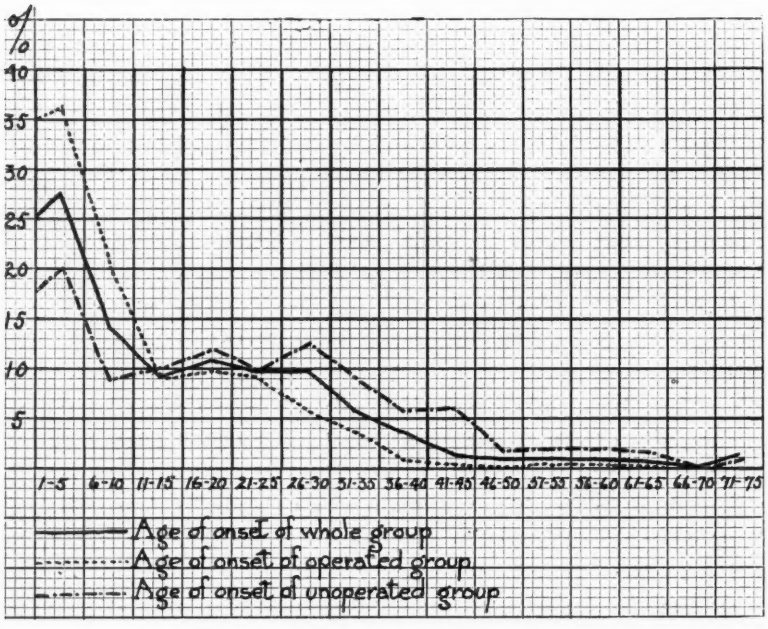

Chart 1.

Chart 1 shows in percentages, by five-year groups, the ages of onset of symptoms of the whole group of 600 patients, and of the group on whom tonsillectomies were done, and of the control group.

Individuals presenting, in childhood, symptoms of disease of the respiratory tract, especially obstructive symptoms, are more likely to have their tonsils removed than are those who wait until adult life to present such symptoms. This is reflected in the fact that 33 per cent of these patients on whom tonsillectomies were done had their first allergic symptoms by the time they reached the age of five years, and 66 per cent began to have manifestations of allergy under the age of

fifteen years, whereas only 40 per cent of the unoperated group had their first symptoms in childhood.

In but a small proportion of the cases was it possible to learn why the tonsillectomies were done. Many patients knew only that their tonsils had been removed in childhood. Others stated that the operation had been done because they had suffered from repeated colds, or from nasal obstruction. In some cases, the tonsils were removed because of the allergic symptoms alone.

It is probable that the most severe cases were subjected to tonsillectomies in order that nothing be left undone which might be of benefit. This is suggested later in the consideration of the results of treatment.

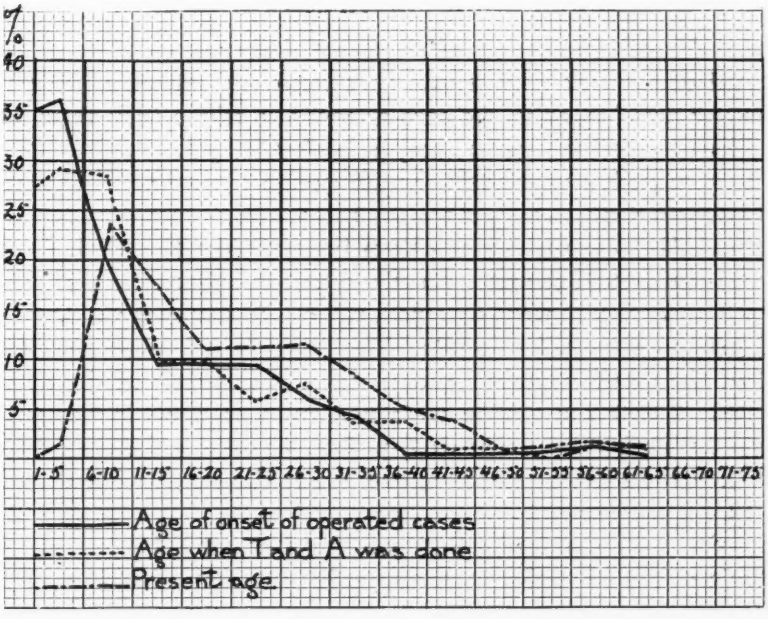

Chart 2.

Chart 2 shows in the same way, the age of onset of symptoms in the tonsillectomized cases; their ages when the operations were done, and their ages when they presented themselves for treatment. Two-thirds of the operations were done while the patients were under fifteen years of age, although adult life did not act as a bar to tonsillectomy.

The relation of the curve denoting the present ages of the patients to that denoting the ages at the time the operations were done indicates that an average of three to five years elapsed between the time of operation and the time when the patients appeared for treatment. It seems proper to deduce that any patients who had been greatly relieved, or cured by tonsillectomy, do not appear in this group.

Eight patients stated that they had received definite benefit from

tonsillectomy, largely in the relief of nasal obstruction. Eight others were benefited for from one to three months. Five thought they were worse after the operation.

TABLE I

RESULT OF TREATMENT

GOOD	FAIR	POOR	FAILURE
OPERATED GROUP			
32.6%	33.4%	12.4%	15.6% (6% refused treatment)
66%			
UNOPERATED GROUP			
31.7%	37.7%	12.0%	16.6% (2% refused treatment)
69.4%			

Table I shows the results of treatment. Treatment consisted in the removal of the offending substances from contact with the patient whenever possible, as in the case of foods to which they were hypersensitive; the animal emanations, as in feather pillows, etc. Patients reacting to pollen were treated with pollen extracts. Most patients who gave no positive skin reactions received treatment with bacterial vaccine. All were given medication for symptomatic relief.

In 66 per cent of the patients whose tonsils had been removed, good to very good results were obtained, while 69.4 per cent of the unoperated group gave similar results. Treatment failed to benefit 15.6 per cent of the tonsillectomized group and 16.6 per cent of the controls.

The fact that the results were not quite so good in the patients whose tonsils had been removed, probably means, as was said above, that they were the worst cases, and is not the result of the tonsillectomies.

Six per cent of the tonsillectomized group, and 2 per cent of the controls either refused treatment, or had so little that it was of no value.

Through the kindness of Dr. Albert D. Kaiser, I have been permitted to study his records covering 2,000 school children. In 1,000 of these children the tonsils had been removed at the age of five or six years. The remainder had been advised to have their tonsils removed at the same age, but for various reasons had not done so. These serve as controls. These children were examined at the time the tonsillectomies were done, or advised to be done, and again at the end of ten years. The incidence of diseases was recorded for both groups. These two groups of 1,000 children were divided among the same schools and came from similar homes. They were similar racially.

TABLE II

INCIDENCE OF ALLERGIC MANIFESTATIONS IN TEN-YEAR FOLLOW-UP

1,000 Children (tonsillectomy)		1,000 Children (controls)
41	Allergic coryza or asthma	36

Table II shows the incidence of allergic manifestations of the respiratory tract in these two groups.

SUMMARY

1. The tonsils have been removed from approximately one-half the children in urban schools.

2. Many laymen, and some doctors, believe that tonsillectomy will greatly benefit, or cure allergic coryza, or asthma.

3. Most authors of books on allergy either do not mention tonsillectomy as a means of treatment, or state that it is of little value, although at least two take the opposite view.

4. The same diversity of opinion appears in the periodical literature.

5. A study of 300 patients, presenting nasal or pulmonary symptoms of the allergic type, on whom tonsillectomies had been done, and of 300 similar patients, whose tonsils had not been removed, is presented.

6. The good results and the failures from treatment were almost exactly equal in the two groups.

7. In a ten-year follow-up study, the incidence of nasal or pulmonary manifestations of allergy, in 1,000 school children whose tonsils had been removed at the age of five or six years, and of 1,000 similar children who had been advised to have their tonsils removed, but had not done so, is shown. A slightly greater number of the children whose tonsils had been removed developed allergic symptoms than was the case in the children who retained their tonsils.

CONCLUSIONS

Tonsillectomy does not aid in improving the results of treatment of nasal or pulmonary manifestations of allergy. Rare exceptions may occur.

Nasal or pulmonary manifestations of allergy are as liable to occur in an individual whose tonsils have been removed as in one who retains his tonsils.

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26 South Goodman.

(*For discussion, see page 391.*)

THE DIRECT SKIN TEST IN ALLERGY*

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IN 1873 Blackley[1] demonstrated that the skin of certain individuals with hay fever was sensitive to pollens applied locally to abrasions of the skin. Smith[2] in 1909 reported the experiments of Rufus Cole who found a similar response in testing the skin of an individual sensitive to buckwheat. No extensive clinical application of the skin test in allergic sensitization was made until after the thorough study of Schloss[3] in 1912 had established its value.

The finding of clinically sensitive individuals giving negative skin tests and individuals without clinical manifestations giving positive skin tests has of late led to considerable pessimism as to the value of the tests. This attitude was intensified when it was found that certain individuals were test-positive to so many substances, particularly foods, that a rational existence was difficult if the indications of the tests were closely followed.

Our studies have been directed toward an analysis of the factors involved in the skin test phenomena and their interpretation in various phases of allergy in children.

1. THE RÔLE OF TRAUMA AND ITS VARIATION WITH AGE

Considerable difference of opinion exists as to the method of testing. The simple scratch or cutaneous test has been advocated by Schloss,[3] Walker,[4] and Peshkin,[5] while the intracutaneous method has been preferred by Cooke,[6] Coca,[7] and others.

We observed very early differences in response to trauma, not only the occurrence of unusual reactions such as factitious urticaria and dermatographia as are noted in the adult but a definite variation with the age of the child tested. As judged by erythema a simple scratch on the skin of a very young infant was attended by considerably greater response than in the case of an older child.

This was studied in a series of nursery, hospital and out-patient children. A simple cutaneous scratch was made with a dulled chalazion knife, on the flexor surface of the forearm. The erythema was measured ten to fifteen minutes afterward. While individual differ-

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ences were still noted and although uniformity of conditions could not be controlled, the variation during the first two years could be told by percentage approximations. The curve in Fig. 1 illustrates the traumatic response in different months of early infancy.

Although we have no exact figures by which to compare the response to trauma in eczematous infants and normal infants, we are of the opinion that the former show an even greater response.

DISCUSSION

The response to trauma of the skin has been studied by Lewis[8, 9] and his coworkers. The erythema and whealing, they conclude, are due to liberation from the skin of a "histamin-like" substance that reacts on blood vessels and nerve endings. Physical agents such as cold, heat, light, etc., may behave in a similar manner. Unfortunately

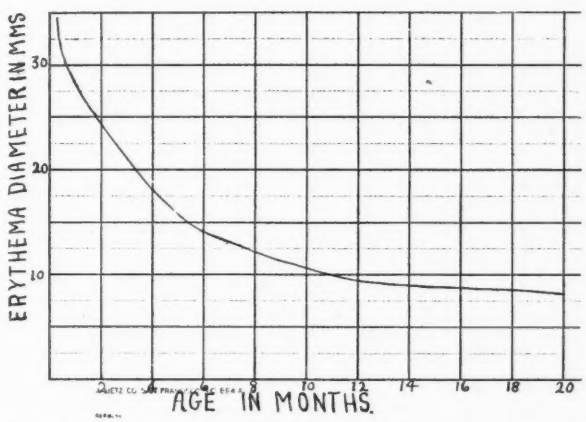

Fig. 1.—Ratio of extent of trauma in skin testing to age of infant.

for comparison with our observations, the majority of their studies have been made on adults; but their investigations of the substance in the skin which promotes the "histamin-like" response have produced some results comparable with ours. Harris[10] made extracts of the human skin and found that they contained a substance which acted in a manner similar to histamin when injected into the skin. Although he did not stress the difference in sources of the skin, examination of his tables shows that when obtained from infant or fetal skin, the extract was uniformly twice or three times as potent as that from adults.

Adelsberger[11] examined the reaction of the skin of children to different irritants such as Bloch[12] has used in the study of eczema. She found that the skin of very young infants responded readily to mechanical stimuli but that the irritants (arnica, quinine, etc.) had no specificity. While the underlying reasons for this heightened response

of the infantile skin are not clear, certain known differences between the adult and infantile skin may be mentioned. Terminal capillaries of the young infant are imperfectly formed and do not resemble the adult loops until the infant is three or four months of age. This may account in part for the wider diffusion of the erythema, the capillaries, as Lewis[8] has shown, being reflexly stimulated by the trauma.

The fat of the infant contains a greater amount of palmitic acid and a smaller amount of oleic acid than that of the adult. These differences are gradually decreased with age. Harris' extracts of the epidermal layer, however, showed a concentration of the reactive substance six times greater than the dermal layer of the skin. From these data we would presume that the difference in fat composition was not concerned in the reaction of the skin to trauma.

Sexsmith and Peterson[13] showed that the enzymes of the skin vary according to age. The young skin contains little protease and more erepsin and peptidase, while in the adult skin the reverse is the case. Usually these findings have been advanced to account for the age variation in reactivity of the skin to bacterial toxins, etc. They may also, however, be concerned with the greater response of the infantile skin to trauma.

2. THE RÔLE OF TRAUMA IN CUTANEOUS VS. INTRACUTANEOUS TESTS

From the preceding discussion it will be seen that trauma plays an important part in producing nonspecific reactions. This is particularly true when the intracutaneous tests alone or without controls are done on children. That the intracutaneous method may be too delicate for children is illustrated by the following case history:

E. H., female, aged ten years. History of allergy in family denied. Onset of asthma at two years of age. Intracutaneous tests, during 1928, gave positive reactions to:

wheat	cloves	feathers
chicken	grapefruit	dog hair
chocolate	pineapple	cotton seed
peach	blueberry	hops
orange	turkey	orris root
nuts	clam	wool
eggs	sea bass	timothy
pepper	smelts	hickory tree
beans	catfish	ragweed
spinach	sardine	tree of heaven
okra	caviar	red top
artichoke	raisins	careless weed
parsley		

Admitted to Children's Hospital Sept. 16, 1929, simple cutaneous tests showed reactions only to:

orris root	goose feathers	horse dander
chicken feathers	duck feathers	cat hair

The patient was in a particularly poor state of nutrition, due, we thought, to excessive dietary restriction. A general diet was allowed without any development of asthma. The parents were urged to place the child in the convalescent home, where a minimum exposure to household inhalants was assured. Under protest, however, she was taken home Oct. 20, 1929. A severe attack occurred immediately. She returned Nov. 12, 1929, to the hospital, and was sent to the convalescent home until May 19, 1930. During her study she gained sixteen pounds and was practically free from attacks. Tests on discharge were precisely those previously obtained Sept. 16, 1929.

Since we were dealing with young children and infants the cutaneous method with a control was adopted for routine. Where reactions were negative or doubtful by this technic, the intracutaneous method was sometimes used. But after the occurrence of two generalized reactions following the intracutaneous tests with egg white, we have never resorted to that method without preliminary cutaneous tests.

3. VARIATIONS IN THE ALLERGIC SKIN REACTION—AGE FACTOR

Considerable attention has been paid to the loss of both skin test and clinical sensitivity with increasing age of the individuals tested. Stuart and Farnham[14] have shown that skin tests to foods are more frequently positive in the younger children, while the tests to inhalants are more common with advancing age. Certain individuals in this group showed a loss of skin reactions and clinical sensitivity to foods but a development of reactions and symptoms referable to inhalants. These observers infer that the hypersensitivity to foods tends to be present at birth and lost during childhood, while sensitivity to inhalants tends to be acquired and is more resistant to change. They do not report, however, tests in infants except as grouped according to the year, by which data they find the greatest number of positive food reactions in the first year.

Concerning the frequency or development of positive reactions during the first year, information is lacking. Clinical reports of very young infants with unquestioned hypersensitivity have frequently been made with study of the skin tests. Of sporadic case studies with positive skin reactions, the youngest we have noted was reported by Lyon[15] in an infant whose symptoms developed at three weeks of age, but whose skin tests were not observed until six weeks of age, at which time they were positive. Park[16] reported a detailed study of

an infant markedly sensitive, but whose skin tests at three months were not clear cut. Subsequent tests at ten and eleven months were doubtful.

In the observations of skin tests in groups of individuals with or without clinical manifestations, information is likewise wanting with regard to the tests in very young infants.

Schloss[17] reported a study of 122 cases of allergy in children. Although a specific instance of positive skin reactions in an infant five months of age is cited, the ages of the infants with eczema are grouped as under or over sixteen months. In the group under sixteen months of age there were 53 cases of whom 40 gave positive reactions. Those over sixteen months were 24 in number, and 10 of these gave positive reactions. Blackfan[18] reported positive reactions in 22 out of 27 patients with eczema whose ages varied from five weeks to forty years. While most of the individuals were "under one year of age" no special attention was paid to relation between age and skin test phenomena. He mentions, however, one infant with positive reactions at five weeks. Talbot[19] mentions 16 cases of whom 14 gave positive reactions, but the incidence with relation to age is not discussed. Twenty-three infants and children with eczema were tested by Sidlick and Knowles.[20] Fifteen gave positive results, the youngest of whom (three months of age) gave weak reactions. Shannon,[21] studying 8 breast-fed infants with eczema, reported the youngest in his group at eight weeks of age. The patient gave "erythematous" reactions to a large number of foods. O'Keefe[22] reported 70 cases of eczema, all under four years of age, the majority being under two years. Forty-one per cent gave positive skin reactions, twelve gave doubtful reactions. Walker[23] in a study of 400 patients with bronchial asthma reported 34 under two years of age developing asthma. While he did not state the age at which he performed the tests, he found 28 of them gave positive reactions.

O'Keefe and Rackemann[24] report more recent observations on 239 cases of eczema in children of whom 125 gave positive reactions. Skin tests were positive in 39 per cent of those in the first six months and 60 per cent of those between six and twelve months of age. They interpret this as indicating that hypersensitiveness to foods is acquired when the foods are first eaten.

In the study of the incidence of positive reactions in the absence of clinical features of allergy, Baker[25] found 4 to 8 per cent positive. He used only food substances for the tests and gave no statistics with regard to the ages of the children tested. Peshkin and Rost[26] reported as high as 10 per cent "doubtful or positive" reactions but claimed that the reactions decreased with age, the youngest group being two to five years. They further claimed that the reactions were usually to foods most frequently encountered in the dietary of children. Blackfan[18] found

only one positive skin reaction in 43 normal individuals. That one instance occurred in an infant nine weeks of age.

Balyeat[27] has recently reported tests on 119 newborn infants. He found two with marked positive reactions. He states that tests are easier to read since there is less traumatic reaction. This we have not been able to verify. Although his report is a study of the hereditary factor in allergy, he does not state whether there was an hereditary background for the newborn group. Subsequent tests on the test-negative infants in that group, or proof of antibody titer by passive transfer in the test-positive cases, were not reported.

DATA FROM OUR SERIES

One hundred and twenty-five newborn infants were tested in the nurseries of the St. Louis Maternity Hospital. The substances used (egg, wheat, and milk) were those which, in the group of older allergic infants and children, most frequently gave positive skin reactions. The entire group was test-negative. In addition, cord blood was obtained from three mothers in allergic families. Passive transfer of this blood was negative, and the infants showed no response to the direct test even in the one case where strong reactions were obtained from the mother's tests. While we believe there may be a possible placental transfer of immune bodies concerned with allergic phenomena in some cases, we have as yet too few controlled observations to substantiate this. Ratner, Jackson and Gruehl[28, 29] have advanced the theory from experimental and clinical material, that the ante-partum diet of the mother may lead to a sensitization *in utero*. In this a placental transmission of the antigen is concerned, not the allergic antibody (skin-test substance) which we are discussing.

In a study of 85 cases of eczema (to be reported later), where skin tests were performed at frequent intervals, we found the following data with regard to tests in infants under six months of age:

Total 6 months or under	27
No. with positive skin reactions	19
Total 5 months or under	21
No with positive skin reactions	8
Total 4 months or under	13
No with positive skin reactions	4
Total 3 months or under	9
No. with positive reactions	2

The youngest in the whole group to give positive reactions was an infant eleven weeks of age. The infant had been tested before at eight weeks, at which time the tests were negative.

While the series is small, there is nevertheless a definite indication that the tests are less likely to be positive under six months.

Twelve of the 85 patients with eczema developed positive skin reactions, when earlier in the period of observations the reactions had been negative. Several of these patients were hospitalized for the observation period, and any contact with the offending food could be ruled out. The following brief résumés will serve to illustrate:

CASE 1.—E. H., male, aged three months, admitted to Children's Hospital Sept. 6, 1929. The father had severe urticaria. The infant's eczema began at three weeks while on the breast. Feedings were changed to a dried milk. No supplementary foods were given.

Tests—milk, egg, wheat:

Sept. 18, 1929, negative
Oct. 5, 1929, egg ? positive
Oct. 28, 1929, egg definitely positive
Dec. 11, 1929, egg definitely positive
Jan. 4, 1930, egg very strongly positive
Apr. 8, 1930, egg very strongly positive
wheat very strongly positive

CASE 2.—C. R., male, aged six months, admitted to Children's Hospital Feb. 16, 1929. Mother has had severe eczema. Infant's eczema began when child was one month old. Skin tests negative at time of admission. Discharged March 2, 1929, on evaporated milk diet. Readmitted May 4, 1929.

Tests: milk +++
egg +++

CASE 3.—D. F., male. Allergy denied in family. Onset of eczema at two months. First seen in Out-Patient Department at five months. Exclusively breast fed until Feb. 20, 1930, when on account of the failure of breast milk to meet the demands of the infant's nutrition, a Sobee formula was given as a complementary feeding.

Tests:

Feb. 6, 1930. Milk, egg, wheat, negative
Feb. 20, 1930. Milk, egg, wheat, faint positive
Mar. 10, 1930. Milk, egg, wheat, strongly positive

It will be seen that so far as the skin tests were concerned, despite the possibility of intolerance to certain foods, these infants gave no positive reactions before three and one-half to four months. About that time the tests showed a slight reaction to certain substances, particularly egg white. Subsequent tests became more marked with the characteristic wheal and pseudopods. While most of these which were carefully followed developed positive reactions by six months, some did not do so until even later, and some not at all. Most of them have retained

their positive tests—one patient for the three years during which she has been under observation.

DISCUSSION

In other fields of immunology, this variation of skin reaction with age has been well established. Rolly[30] found that infants failed to react to bacterial toxins but developed reactions with increasing age. Tezner[31] showed that as the skin of children became increasingly sensitive to bacterial toxins, a corresponding sensitivity was noticed for such substances as Witte's peptone. Very recently, Freund[32] has shown that agglutinin, hemolysin and precipitin formation is weak and difficult in young rabbits, but increases with advancing age. We believe that this "Umstimmung" follows a general immunologic law and has its analogous effect in the development of allergic skin tests in infants.

However, the belief that this phenomenon is related to increasing exposure to the antigen is, in the case of the allergic infant, difficult to prove. There is, as yet, no evidence that the breast milk secretes the antigen (experiments to be reported) and in the cases under our observation no possible contact has been found. Indeed, with egg white, the substance most frequently producing reaction, it is difficult for us to accept the conclusion that "it points to an acquisition of sensitivity for foods most frequent in the infant's diet." The stimulation may, of course, have come from placental transmission of the antigen, as suggested by Ratner.[29] The development of the skin test antibody, however, is not manifest until three or four months of age—a situation somewhat analogous to the development of the Wassermann reaction.

4. OTHER FACTORS APPARENTLY AFFECTING SKIN TESTS

Stuart and Farnham[14] have shown that there is a general tendency to develop negative skin tests to food at about eight years of age, while tests to inhalants become increasingly more frequent. Whether this is related to a graded increase of tolerance is not entirely clear. But aside from this general trend, variation in the skin reactions has been noted in other situations. Schloss[17] reported the disappearance of skin reaction to egg after the individual had a severe upset from oral ingestion of egg. He also reported negative tests following graded therapeutic administration of egg where no severe clinical reaction was occasioned. In the first instance the loss of skin tests was temporary, somewhat analogous to antianaphylaxis; in the second, the term "desensitization" has been applied. Coca[33] objects to the use of this term and claims an increase in skin reaction after graded administration. Lamson, Piness and Miller,[34] however, have not confirmed Coca's claims.

In the group of children under our observation we have noted negative skin tests apparently related to the following causes:

a. Severe generalized reactions.
b. Graded therapy.
c. Freedom from contact.
d. Drug therapy.
e. Faulty preparation of the antigen.
f. Inability of individual to form skin-test antibodies.

a. Severe Generalized Reactions.

C. B., aged four years, male. Family history not clear. Complaint: asthma. Patient had eczema in early infancy. Asthmatic attacks started at two and one-half years, and occurred about every four weeks. No seasonal variation. Admitted to Children's Hospital Sept. 20, 1928. Physical examination showed a rather poor state of nutrition and diseased tonsils. Skin tests gave marked reactions to wheat, egg and oats in the food group, and to feathers, house-dust and ragweed in the inhalant group.

The boy was placed on a restricted diet and before discharge the home had been rid of all feathers. He did well after discharge for about three months. At that time the parents took him for a day to the home of a friend. He played for twenty minutes with feather pillows on a couch, and then was seized with sneezing and coughing, followed by urticaria and asthma. He was brought to the hospital as the attack was subsiding. No epinephrin was given. Skin test to feathers was negative on Feb. 5, 1929. On May 28, 1929, test to feathers was again positive.

Although we have observed the persistence of skin tests in other instances of severe reaction, we believe that there are fluctuations in the antibody titer in which it is difficult to escape the conclusion that severe reactions may be followed at least temporarily by negative tests.

b. Graded Therapy.

E. A. S., aged three years. Patient had eczema starting at four months. Tests to cow's milk, egg and wheat at four and one-half months were positive. Dryco formula was given. At six months rice and carrots were started. Tests repeated were still positive. At twelve months tests were still positive but reaction to cow's milk was less pronounced. A formula of cow's milk boiled for four hours was gradually substituted for the Dryco. At eighteen months tests were still positive, though the clinical improvement first noted with Dryco feeding was maintained. The length of time for boiling the milk was gradually lessened until at twenty-two months, milk that had been boiled five minutes could be given. Tests to milk were negative at that time while those to egg and wheat were still positive and surreptitious ingestion of bread was followed by severe reaction.

c. Freedom From Contact With Offending Substance.

D. C., aged four years. Maternal aunt and uncle had asthma. Patient had eczema in early infancy and urticaria at two years after playing with an egg beater. "Choking spells" periodically occurred during the first year, but the asthmatic nature of these attacks was not recognized until two years of age.

Apr. 25, 1929. Patient was first seen following an acute attack, at which time all tests were negative. Trial diet was started and advice given concerning the avoidance of household inhalants. May 24, 1929. Tests showed slight reaction to egg white. Fair improvement was noticed for the next few months until an acute infection (otitis media and pharyngitis) associated with a mild attack of asthma brought child to hospital.

Tests showed very marked reactions to house-dust, duck feathers, cat hair, and ragweed. Social service follow-up revealed rather poor home cooperation so far as riddance of inhalants was concerned. Patient was then sent to convalescent home, Nov. 15, 1929. After seven months with practically no attacks and with considerable improvement in weight and physique, she was discharged home on June 7, 1930. Tests at this time showed only slight reaction to cat hair.

d. Drug Therapy.

We have seen what appears to us to be a transient interference due to epinephrin. For example:

E. H., female, ten years of age. Previously tested Oct. 5, 1929, at which time positive skin tests were obtained to orris root, cat hair, chicken, duck and goose feathers and horse dander. Readmitted to the hospital after an interval at the convalescent home. By error the patient was placed on a horse-hair mattress (instead of the washed moss type used for asthmatics). A mild asthmatic attack occurred during the night, for which epinephrin (6 minims) was given. Tests were negative the following morning. On the second morning the tests were repeated and strong positive reactions were obtained to orris root, cat hair, chicken, duck, goose feathers, and horse dander.

We have observed a similar effect in other patients. However, this reaction to epinephrin cannot be obtained constantly even in the same individual.

e. Faulty Preparation of Allergen (Test Substance).

The substances used for testing may be at fault. It has frequently been observed that foods may be altered particularly by cooking so that they no longer give clinical manifestations. Many children will have urticaria from fresh strawberries but will have no difficulty with cooked strawberry jam. Schloss[17] refers to boiled, evaporated or dried milks as "denatured" and Kerley[35] has advocated prolonged boiling of milk for feeding infants with eczema.

That the process of extraction and preparation of the test substance may likewise influence the skin response on testing is illustrated by the following case:

J. D., known clinically sensitive to fig. Tests both cutaneous and intracutaneous with prepared powder and extracts were negative. Fresh fig juice placed on a simple cutaneous scratch produced very definite wheal and erythema.

f. Absence of Skin-Test Antibodies.

We have not found many such instances of the preceding phenomenon. In one family where sensitivity to orange was discovered by "trial and error" diets, the tests were repeatedly negative, whether fresh fruit juice, extract, or powder was used. Another patient with positive tests to egg and tomato, to which the child was also clinically sensitive, gave negative reactions to orange regardless of the fractions or preparations used. In a study of eczema to be reported we found 17 in the total of 85, who failed to give the slightest reactions to substances tested. Contributing factors such as skin infection, sensitivity to cold, heat, etc., were not present. Yet by eradication of substances most usually positive in those giving skin-test reactions, very satisfactory results were obtained.

J. S., aged two and one-half years. Maternal grandfather had hay fever; mother had eczema. Onset of eczema at two months. Frequent attacks of abdominal pain. Private physician prescribed "vegetarian" diet without relief. Tested by us April 12, 1930, to various foods and inhalants with negative results. Given egg, wheat, oat, and potato-free diet, evaporated milk being allowed. Seen April 26, 1930, with great improvement. Tests were negative. Oats were tried with resulting flare-up of eczema. On May 17, 1930, retested with negative results; wheat added to diet with return of eczema and abdominal cramps. Potato was added to the diet on May 31, 1930. This was followed by prurigo and a return of the skin eruption.

This protocol shows quite clearly the presence of a definite sensitivity without skin-test manifestations. In a subsequent report we mention further evidence to show that, while usually related, the skin-test phenomena and the capacity to react clinically are independent variables.

SUMMARY

1. The skin of younger children and infants gives a greater response to trauma than does that of older individuals. This may be due to liberation of a toxic substance in the skin cells.

2. Clinically this finding may interfere with the interpretation of specific allergy tests, particularly when the intracutaneous method is used.

3. Specific skin reactions dependent on an antibody presence (reagin of Coca) are rare in infants under four months, regardless of sensitivity or contact with allergen. With increasing age, the antibody likewise increases, apparently following a general immunologic law.

4. Skin tests may become negative following these conditions:

(a) Severe allergic reactions.
(b) Graded therapy.
(c) Freedom from contact.
(d) Epinephrin administration.

Skin reaction may also fail because of faulty preparations of the test substances (allergens) or because of inability of the individual to form the skin test antibody, even though he is clinically sensitive.

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VERNAL CONJUNCTIVITIS

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PHILADELPHIA, PA.

VERNAL conjunctivitis, or Frühjahrskatarrh, is characterized clinically by redness of the eyes, itching, lacrimation, frequently by a lardaceous discharge containing eosinophiles. Pathologically, there is a hyperplasia of the follicles of the conjunctiva of the upper lid and rarely of the lower lid; or it may manifest itself as a vesicular eruption discrete or confluent at the border of the cornea. Both eyes are involved but not necessarily at the same time.

Its onset as observed in Philadelphia is always from April or May to August, never beginning in the fall or winter months, but once having developed in the spring or summer, it may continue throughout the year in the lid type only and never in the limbic or corneal type. The symptoms, itching, lacrimation, and mucous discharge, may return in the winter when the patient is exposed to unusual heat, but the symptoms on such occasion are only trivial and never approach the type of distress experienced in the hot summer months. The corneal type always disappears completely both symptomatically and pathologically with the approach of cold weather and is never seen during the fall or winter months.

The disease occurs principally in children five to ten years of age, rarely under five years and frequently among adults as a primary disease or as a chronic disease from childhood.

Of the 70 cases studied during the last seven years at the Wills Hospital and in private practice, 73 per cent were among males and 27 per cent females. This compares favorably with Posey's[1] report of 85 per cent males and 15 per cent females. Forty-two cases were of the lid type, and 28 of the corneal type.

Forty-one per cent were in the age group ten and under (only two cases under five); 30 per cent, eleven to twenty years; 20 per cent, twenty-one to thirty years; and 9 per cent, over thirty years. In 30 cases conjunctival smears were made. Twenty-two revealed eosinophiles; 15 of these were lid types and 7 corneal types; the highest count was 49 per cent. Blood counts were performed in 40 cases. Twenty revealed an eosinophilia over 4 per cent, the highest count being 16 per cent. Fourteen were lid types and 6 corneal.

There was no striking family history of the common forms of sensitivity. While several cases gave histories of hay fever or asthma in the family, they were not numerous enough to be impressive. Some

*Read before the Seventh Annual Meeting of the Society for the Study of Asthma and Allied Conditions, Atlantic City, May 2, 1931.

patients spoke of aunts and uncles having had hay fever or asthma, but pressed for definite information, they were uncertain about it.

A definite finding, however, is the fact that in no instance was a second case of vernal conjunctivitis found in other members of the family.

The duration of the disease is at least two seasons, the average being three years, but many cases last five to ten years, rarely longer. The oldest patient in this series is fifty-eight years old, having had seasonal attacks since early childhood. The youngest patient is one year old.

TYPES OF VERNAL CONJUNCTIVITIS

There are two distinct types of vernal conjunctivitis, the lid type and the corneal. They differ from each other in location of the pathologic lesions and in the character of symptoms. The limbic or corneal variety is characterized by discrete vesicles, one, two, three or more, occurring about the rim of the limbus. Crops of vesicles may become confluent, forming a crescent gray frosting over the upper half of the rim of the limbus, or it may completely encircle the corneal border. The conjunctiva of the lid and eyeball may be hyperemic. The vesicular eruption is completed within the first few weeks of the disease. The itching is not so intense as in the lid variety. The discharge is scant and watery. The symptoms and the pathology disappear entirely with the approach of cold weather in September. Recurrences never occur during the winter months. The visual acuity is never affected by this disease.

There are three distinct varieties of the lid type:

1. Simple follicular,
2. Cobblestone,
3. Giant granuloma.

The *simple follicular* type does not have any pathologic identifying characteristics. It resembles follicular conjunctivitis in appearance, and clinically, there are the "bloodshot" eyes, the lacrimation, and mucous discharge, and itching.

The *cobblestone variety* is the advanced stage of the disease, and is characterized by the pavement or cobblestone appearance of the follicles on the upper lid. There is also seen a milky appearance of the conjunctiva of the inverted lids, upper and lower. The discharge in this variety is characteristic, there being no other ocular disorder having a similar exudation. It is a thick, ropy, lardaceous discharge, which peels off without bleeding in large clumped masses. Microscopically, it reveals the presence of mucus, epithelial cells, mononuclear leucocytes, eosinophiles, and polymorphonuclear leucocytes. Shunway claims that the staphylococcus is frequently found in this discharge.

Giant Form.—The large granuloma type is also an advanced stage and is rarely seen. It is an exaggerated form of the cobblestone variety in which the granulations become unusually large.

The intensity of the itching bears no relation to the extensiveness of the pathologic lesions. The patient with few follicles or granulations may experience more troublesome itching than those patients with large follicles or extensive corneal involvement. The itching is most severe at sundown or early evening, or it may develop suddenly after exposure to sunlight, after swimming, or excitement. The symptoms are most disturbing on very hot, humid days.

Not one case in the present series showed the coexistence of the lid type and the corneal type. In no instance was the lid variety found in negroes.

ETIOLOGY

Conflicting opinions have been rendered regarding the cause of vernal conjunctivitis, many with very little or no convincing evidence to substantiate them.

Rosica[2] ascribes it to an endocrine imbalance, especially a deficiency in the secretion of the suprarenals.

Rizzo[3] studied eleven cases with special reference to constitutional factors. "Practically all the patients showed physical anomalies, including eunuchoid type, infantilism, and degenerative signs in secondary sexual characteristics. In four cases a status lymphaticus was demonstrable. There were also present in various groupings, signs of vagotony, eosinophilia in the blood, and relative lymphocytosis . . ."

Baldassare,[4] believing vernal conjunctivitis is a disease of individuals of vagotonic constitution, obtained relief in three cases following three to five injections of adrenalin.

Sanguinetti[5] has collected statistics regarding vernal conjunctivitis in various localities with a view to discovering whether a recrudescence in Florence should be attributed to exceptional heat and dryness. His conclusion is in the affirmative.

Lemoine[6] reports a pollen reaction to vernal conjunctivitis and a reaction to wheat and eggs.

The first systematic research on vernal conjunctivitis in connection with pollen sensitivity was reported by Fort and by Townsend in 1923.

Fort[7] found five cases of vernal conjunctivitis which reacted to spring pollens and four to autumn pollens. He treated eleven cases with spring pollen and four with fall pollens. He obtained one cure, thirteen cases were improved and one case was lost.

Townsend[8] states that he believes vernal conjunctivitis to be an anaphylactic reaction similar to that of hay fever, asthma, or some types of urticaria and eczema.

I[9] reported five cases of vernal conjunctivitis observed in 1924, which reacted either to the grasses, animal dusts, or foods.

In determining the sensitivity of patients, I have used the 2 per cent liquid extracts of grasses and trees, applying the scratch method. Realizing that this method was not so accurate as the intracutaneous, and being cognizant of the fact that an ophthalmologist is not an expert in interpreting reactions, I invited Dr. J. Alexander Clarke to make a study of certain cases, the results of which are given in Table I.

TABLE I

JEFFERSON NO.	2726 B	2730	2727 B	2720	2726 A	2721	2718	2727 A
Family History	+	+		0	0	0	0	0
Grass	±	0	+	++	+	0	0	0
Ragweed	++	0	+	0	0	0	0	0
Plantain	±	0	+	0	0	0	0	0
Sheep Sorrel	±	0	+	0	0	0	0	0
Poplar	±	0	0	0	0	0	0	0
Oak	±	0	0	0	0	0	0	0
Sycamore	±		0	0	0	0	0	0
Willow	±	±	0	0	0	0	0	0
Maple	+	0	0	0	0	0	0	0
Alder	±		0	0	0	0		0
Hickory	±	0	0	0	0	0		0
Elm	±			0	0	0		0
Ironwood								0
Ash	±			0	0	0		0
Butternut						0		0
Birch	0			0	0	0		0
Walnut			±		0	0		0
House Dust	+	+	+	+	+	0	+	+
Orris Root	0	±	0	0	0	0	0	0
Chicken Ep.		0	0	0	0	0	0	0
Duck Ep.		±	0	0	0	±	0	0
Goose Ep.		0	+	0	0	±	0	0
Dog Ep.	+	0	±	±	0	0	0	0
Cat Ep.	+	0	±	±	0	0	0	±
Cottonseed Meal		0	0	0	0	0	0	0
Wheat			0	0	0		0	
Horse Ep.	0	0	±	0	0	0	0	±
Buckwheat			0		0			
Rice		0	0		0		++	
Cornmeal			0		0		0	
Rabbit							0	
Pyrethrum							0	
Spinach							+	
						7 Vegetables	0	

REPRODUCTION OF THE CLINICAL SYMPTOMS OF VERNAL CONJUNCTIVITIS

At the suggestion of Dr. Arthur Coca and Dr. J. Alexander Clarke I introduced the exciting agent into the conjunctival sacs of two patients who had vernal conjunctivitis during the summer months, but who had no clinical symptoms during the winter.

In the first instance, H. L., aged seventeen years, was found to be sensitive by the scratch method to June grass, orchard grass, red top, and timothy. The second case, J. S., aged eighteen years, was sensitive to June grass, timothy, rye grass, orchard grass, and maple. On three different occasions during the month of February, I instilled

these exciting agents in one eye of the respective patients. In Case 1, hardly a minute had elapsed before the patient excitedly complained of severe itching in the inoculated eye. Within fifteen minutes, the conjunctiva became intensively injected, red, and edematous. Lacrimation became profuse and the patient became alarmed by the itching. After one hour, a smear was taken of the conjunctival discharge. The laboratory reported the presence of eosinophiles. In the second instance, the exciting agents, including maple, were introduced in one eye, permitting the opposite eye to act as control. Fully twenty

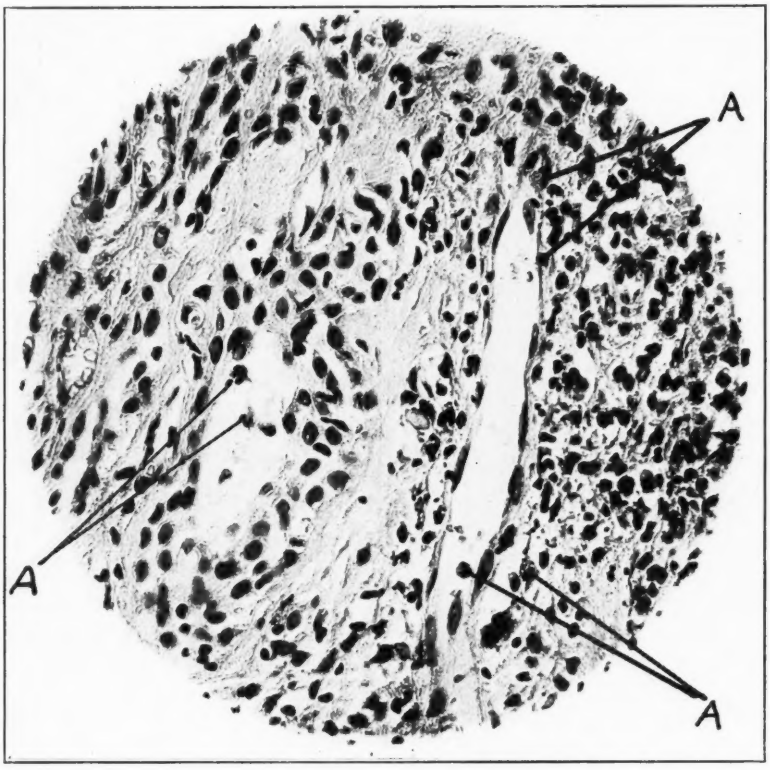

Fig. 1.—High power photomicrograph of tissue from a case of lid type. *A*, eosinophiles.

minutes elapsed before the redness became apparent, associated with lacrimation and the formation of a thin, ropy discharge, which was found to contain eosinophiles. The patient admitted a sense of itching, not very severe. Both patients stated that the irritation of the eye continued for several hours. Four patients who had vernal conjunctivitis the previous summer, but who gave no positive reactions to these same excitants, were used as controls. The same instillations were made in their eyes in the effort to rule out the fact that the pollen extracts were not in themselves chemical irritants. In all of the control patients, no symptoms developed. There was not even a

suggestion of redness. The extract in these cases was that produced by the Arlington Chemical Company. These same four cases of vernal conjunctivitis, acting as controls, were tested for Philadelphia house dust supplied by Dr. Alexander Clarke. One had a very moderate reaction, while the other three were definitely positive. It may be reasonable to suppose that house dusts were the complicating factors in the latter cases.

I am not as yet prepared to speak about the treatment by pollen extracts or by the use of house dust, but I anticipate, before a sub-

Fig. 2.—Low power photomicrograph showing area from which Fig. 1 was taken.

sequent report is made, that the results will be similar to the treatment of hay fever and asthma, except that the best results will be obtained in the limbic forms where complicating infections are not so likely to occur.

PATHOLOGIC REPORT OF A CASE OF LID TYPE

(By Dr. Jefferson H. Clark, Philadelphia General Hospital)

Specimens submitted consist of four small bits of tissue, the largest being 1 mm. in diameter. These were blocked and sections cut in one plane, remounted and other sections cut at right angles to the original ones.

Microscopic examination showed essentially the same histologic examinations in all sections:

(1) The epithelium was of irregular thickness and somewhat edematous, showing occasional goblet cells overlying (2) connective tissue stroma of varying density and complexity. Many areas are sclerosed and show an early hyaline change. This is present not only quite deep in the subepithelial tissue, but also just beneath the epithelium. Other areas consist of younger fibrous tissue, indicated by larger cells with vesicular nuclei. This fibrous tissue stroma shows (3) numerous capillaries, clearly defined by a single layer of epithelium (well illustrated in both high and low power photomicrographs) and (4) simple glands scattered throughout and lined by epithelium of varying thicknesses, resembling that covering the surface. In the lumen of these glands can be found (5) eosinophiles illustrated at "A" in high power photomicrographs. The eosinophiles are also present throughout the stroma, but are not so numerous as (6) round cells, both lymphatic and plasma in type, being more numerous in the areas composed of younger fibrous tissue.

Histologically the specimens resemble tissue the seat of a subacute and chronic inflammatory reaction.

TREATMENT

Various measures for the relief of the itching have been advocated. A solution of zinc sulphate, one grain to the ounce, will give relief, frequently, in the limbic form while the lid types will require the addition of camphor water. Boroglyceрid has been used with satisfaction for a number of years. Others use glycerite of tannin, estevin, fibrolysin, while still others claim results from the use of silver nitrate applied directly to the lids. Still others have used applications of salicylic acid. It should be borne in mind, however, that applications of cold water will also give relief from itching, at least temporarily. Some authorities have used adrenalin subconjunctivally, and others have administered a preparation of calcium intravenously.

I wish to speak, however, of the treatment which I have given in the clinic of Dr. Burton Chance. It is most important in treating these cases to remove all mucous discharge from the eyes. In mild cases, holocain in 1 per cent solution, instilled at the time of severe itching, will give some degree of comfort. In the limbic types, with very little itching, I am satisfied to use zinc sulphate, one grain to the ounce. Where the itching is most intense, boroglyceрid, applied to the lids, daily, will give some relief.

Inasmuch as a calcium deficiency has been found to exist in patients sensitive to proteins, and that calcium administered to such patients relieves symptoms by decreasing the permeability of blood vessels, it occurred to me that the administration of calcium or parathormone (a parathyroid product) would be helpful in vernal conjunctivitis.

Parathormone was reserved for future experimentation. Calcium gluconate (Sandow) was given in heaping teaspoonful doses (90 grains approximately) in orange juice or milk, one-half hour before each meal. Ten patients carried out this treatment during the hot weather in 1930. Each and every one returned regularly asking renewal of the "powdered medicine" expressing the belief that marked relief of itching was experienced. It is difficult to arrive at any definite conclusion, except from the subjective reports of patients regarding symptomatic relief. No detail testing was done to determine the calcium content of the blood before or after administration. On the advice of Dr. A. Cantarow of the Jefferson Hospital, who has done considerable work on calcium metabolism, such determination would be not only difficult, but unnecessary. The large doses of calcium were suggested by him on the grounds that an excess of calcium would not be taken up by the blood and that it was natural to strike a balance of calcium content.

Along with other measures of relief, I believe calcium has some value in alleviating the ocular symptoms of vernal conjunctivitis by reducing the permeability of the vessel walls, reducing the redness, the exudation, the lacrimation, and the itching.

In fifteen cases treated by radium under my supervision at the Wills Hospital, I conclude that radium will give relief from symptoms, will reduce the extent of the pathologic lesions, but will not cure the disease.

SUMMARY

1. Vernal conjunctivitis is an ocular manifestation of an allergy.
2. Two distinct varieties exist.
3. The initial attack always begins in the spring or summer.
4. The pathology of the lid type may persist throughout the winter.
5. The limbic type is never seen in winter.
6. Radium relieves symptoms and changes the pathology but does not cure the disease.
7. The treatment of this disease belongs to the allergist.

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(*For discussion, see page 395.*)

A SURVEY OF THE POLLEN FLORA IN BALTIMORE DURING 1929*†

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WITHIN recent years American allergists have given increasing attention to the pollen content of the air and to its relation to the incidence and treatment of hay fever and asthma. More or less systematic surveys have been made, in various sections of the country, to determine the kinds of pollen present in the atmosphere and the relative abundance of the various kinds during the hay fever season. Among such surveys are those of Durham,[2] Koessler and Durham,[3] Duke and Durham[1] and Moore and La Garde.[4] All were carried on in the Middle West. These workers have developed a technic for catching, counting, and identifying the pollens. The paper of Moore and La Garde[4] includes keys for the identification of pollens. With the help of these keys any person moderately skilled in microscopy, even though he is unfamiliar with botany, may make identifications with reasonable certainty.

So far as we have been able to ascertain, no intensive systematic survey of hay fever pollens has hitherto been undertaken in the East. The present survey was started in 1927, and continued in 1928. It was pushed more intensively in 1929-1930. The method used was a combination and modification of those of the workers mentioned above. Ordinary microscope slides, greased lightly with vaseline, were exposed outdoors. These were collected after twenty-four hours' exposure, and the number of pollen grains, of each species, adhering per square centimeter was determined. The slides were exposed under small sheet metal shelters, open at the sides. These protect the slide from the direct impingement of raindrops, and reduce fouling by large particles of soot and dust, without impeding lateral currents of air. The larger particles of soot and dust tend to settle vertically, while pollens, especially of the dry types which are the most serious causes of hay fever, float easily and are carried more or less horizontally by the lightest of breezes. A comparison of slides completely exposed with slides placed in the shelters showed that the shelters had little or no influence on the number and kind of grains collected.

*From the Protein Clinic of the Medical Department, the Johns Hopkins Hospital, and the Department of Botany of the Johns Hopkins University.

†This investigation was made possible by the kindness of Mr. Joseph Pultizer, St. Louis, Missouri.

Stations at which pollen "traps" were placed were located as follows:

Station R at the Gay residence. This is well north of the city, in the midst of typical eastern Maryland countryside.

Station U in the tower of Gilman Hall, on the campus of the Johns Hopkins University. This is located north of the center of the city, in the midst of a large residential and apartment district. Much of the campus is heavily wooded, and the entire district bears an unusual number of large trees, chiefly oaks and tulip trees.

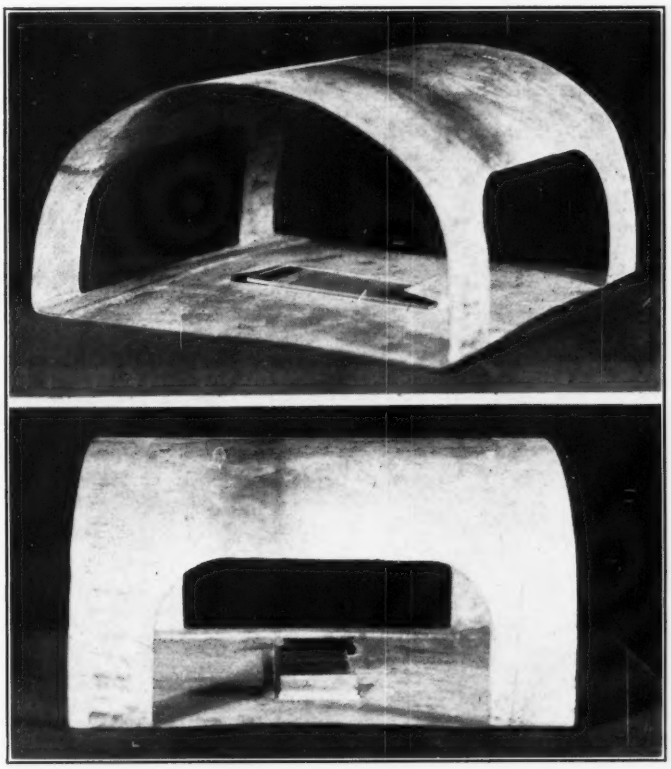

Fig. 1.—Pollen shelter.

Station W at the Acquarone residence, east of the university, near the Baltimore Stadium. Near this section are broad expanses of dry open fields, bearing a heavy crop of orchard grass (*Dactylis glomerata**), other grasses, ragweeds, goldenrods, etc.

Station O on the roof of the Customhouse, in the heart of the business and commercial district, as far removed as possible within the city from the source of the pollens. This station was maintained on

*Botanical nomenclature in this article follows the seventh edition of Gray's *Manual of Botany* (American Book Co., 1908). Cultivated plants not listed in this manual, are named according to "Standardized Plant Names." (De La Mare, 1923).

the instrument platform of the Baltimore Station of the U. S. Weather Bureau.

Station G at the Carr-Lowry Glass Co., on the extreme south edge of the city. This plant is on the water front, near extensive reed and sedge marshes.

These stations extend roughly in a north and south line, nearly at right angles to the prevailing southwesterly winds.

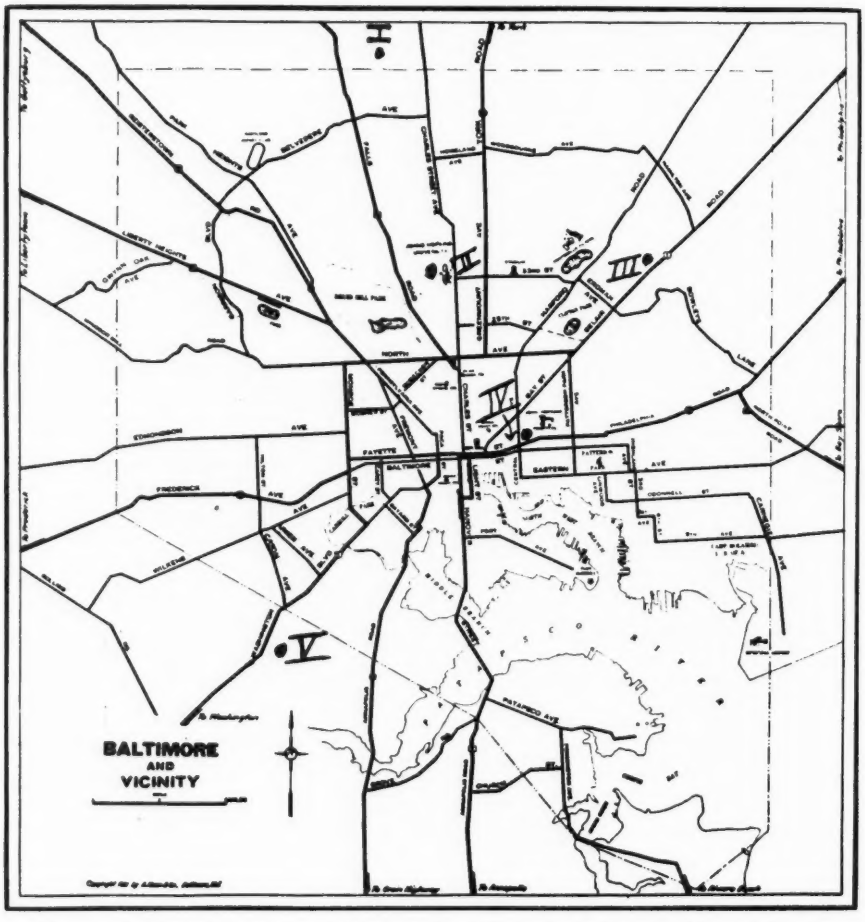

Fig. 2.—I, Station R (Gay residence); II, Station U (Johns Hopkins University); III, Station W (Acquarone residence); IV, Station O (Customhouse); V, Station G (Water front area—Carr-Lowry Glass Co.).

At each of these stations the slides were changed daily, at about 9 A.M., from March 15 to October 31, 1929. They were collected and examined once a week.

METHOD OF COUNTING POLLENS

The reports on most previous pollen surveys give the number of pollen grains falling on an area of 0.55 square inch per twenty-four

hours. This is an area difficult to visualize, even by a person familiar with English units of measurement. To a continental European reader such an area would mean very little. However the counts are made, they should be reported as the number of pollen grains per square centimeter per day.

In making the counts reported here the authors used a Bausch and Lomb microscope with standard 16 mm. and 4 mm. objectives, and a 10 ocular. The microscope was provided with a mechanical stage, to make sure that the slide was moved in a straight line. While observing a stage micrometer through the 10 ocular and 16 mm. objective, the draw tube was extended until the diameter of the field was 1.515 mm. in diameter. The draw tube length was then noted, and counts were always made with the tube set at this length. With most microscopes this tube length is about 160 mm., the length for which microscope lenses are corrected. This is advantageous in observing the finer details of pollen grain walls.

With a field of this diameter (1.515 mm.), three sweeps from edge to edge of a square or oblong cover glass 22 mm. wide cover an area of almost exactly 1 sq. cm.

$$1.515 \times 22 \times 3 = 99.99 \text{ sq. mm.}$$

Due to minor variations in the width of cover glasses (reduced as much as possible by using a supply of carefully measured squares) and to the difficulty of measuring the diameter of the field accurately, a small error is unavoidable, but such an error is insignificant in a study of this type.

Counts were always made under this cambination of a 10 ocular and 16 mm. objective, but a 4 mm. objective, parfocal with the 16 mm., was used for examining grains of doubtful identity. The figures recorded were three times the average count of six or eight sweeps across each preparation. The records were kept in a card catalog. Chart 1 shows a card selected at random from this catalog.

JUNE 2. COOL; N. W. WIND

Stations:	R	U	W	O	G
Dactylis glomerata	18	17	67	30	29
Poa pratensis	10	--	9	2	3
Pinus sp.	--	5	4	1	--
Lolium perenne	7	--	9	--	5
Plantago lanceolata	17	8	12	14	27
Oak hairs	22	56	25	17	31
Spores	6	14	11	10	16
Rumex acetosella	11	3	2	--	14

Chart I.—Sample record card.

METHOD OF IDENTIFYING POLLEN GRAINS

Identification of pollen grains on the slides must be based almost wholly on morphologic features, since the chemical tests described by

Moore and La Garde[4] are hardly applicable to a preparation undergoing careful counting. Identification was based on such criteria as size and shape of cells, thickness and sculpturing of the walls, and number, size, character, and location of pores. (See, in this connection, Moore and La Garde[4] and Pope.[5]) The latter feature is especially valuable, but the pores are sometimes difficult to distinguish, and the presence or absence of a cover or plug in the pore is often scarcely determinable without staining. For this purpose the acetonigrosine stain of Moore and La Garde[4] proved very useful, but we preferred a modification of this stain. Acetonigrosine is simply a solution of nigrosine in dilute (2 per cent) acetic acid. The acetic acid penetrates the pollen grain rapidly, causing the dry grain to swell to its normal size and shape. The nigrosine diffuses more slowly, in a cone, through the pores, and the number and relative size of the pores are determined by counting the cones and noting their size. If covers or plugs are present on the pores, they filter out the nigrosine and become stained a jet black, making them readily visible. It was found that a solution of nigrosine in dilute lactophenol* possessed the staining properties of acetonigrosine, and in addition "cleared" the grains somewhat, which proved of value in observing details. The glycerine content prevented desiccation of the preparations, so that an interesting slide could be laid aside and examined again even after an interval of several weeks. The "lactophenol nigrosine" solution consisted of 0.1 gram of nigrosine (Grübler) dissolved in 100 c.c. of 20 per cent lactophenol. This was allowed to stand twenty-four hours, with occasional shaking, and was then filtered through paper. The solution was kept in a dropper bottle, ready for instant use. A large drop was placed on the slide to be examined, and a clean cover slip was floated on it.

The keys developed by Moore and La Garde[4] proved of great value in making identifications, but we verified each by tracing the pollen to its source (this was possible in all cases except some of the conifers) and comparing the grains on the slides with grains obtained by dissection from mature but unopened anthers. It is obvious that pollen grains which appear on the slides in considerable numbers must come from plants which are abundant and are flowering freely. This makes it easy to trace pollens, in most cases, to their source. One has only to note what species are pollinating abundantly, and to secure pollen of each directly from the anthers in order to obtain standards for comparison with the unknowns on the slides. Pollen grains, the microspores of seed plants, possess, in common with plant spores in general, a high degree of specificity—that is, each species possesses distinctive spores. Color, shape, size, thickness of wall, sculpturing of the wall, pores in

*A mixture of lactic acid, phenol, glycerine, and distilled water, often used in botanical laboratories as a temporary clearing and mounting medium. (See Bot. Gaz. 77: 343, 1924.

the walls, plugs in the pores, cell contents, reactions to reagents or to organic dyes or combinations of dyes are features which are only slightly variable in the spores of any given species, and by noting some or all of these features in pollen grains their identity may be established. In general there are generic and family resemblances in pollen grains, as may be noted in Miss Pope's paper,[5] but there are also specific differences. The differences are sometimes so slight that they are discoverable only by statistical methods. These are often used in a routine way in mycologic taxonomy, where spore characters are sometimes the only features sufficiently fixed to be of diagnostic value in determining species. Pollen grain characteristics can be used in identifying and differentiating species of flowering plants, and are occasionally so used. Since the characteristics of spores are so definitely fixed in each species, it is clear that it should be possible to identify pollen grains with reasonable certainty. Positive identifications to the genus are usually made with little difficulty, except in some of the grasses. Specific identifications can usually be made, but it is often more difficult, especially in the case of trees, as is discussed below.

We were interested in checking the accuracy of the descriptions of pollens by Moore and La Garde[4] and found them on the whole quite accurate and trustworthy, with the exception of those of some of the tree pollens, especially the oaks. Without implying that their descriptions of the latter are actually erroneous, we nevertheless found it difficult, sometimes impossible, to identify some of the oak pollens by means of this key. While oak pollens are fairly distinct generically, specific differences seem inconstant. To a lesser degree this was also true of pollen of other arboreal genera, such as *Acer* (the maples and box elder) and *Populus* (the poplars, cottonwoods, and aspens). The difficulty of identifying oak pollens positively is due perhaps to the fact that the species of oaks, especially the red and black oaks, are poorly defined, and hybridize freely, producing many intermediate types, with intermediate and aberrant types of pollen. This is also true of the poplars. For example, the "Carolina poplars" (*Populus eugeni*) so widely used as shade trees, are hybrids, derived by the crossing of at least three different species of *Populus*, and at least four morphologically distinct types of pollen could sometimes be obtained from a single anther. Positive identification of pollen, to the species, is in such cases impracticable, though not necessarily impossible.

Fortunately for the allergist, and for his patients, this is not an insuperable difficulty. Pollen can usually be traced with certainty to the genus, and it seems to be generally true that a person sensitive to pollen of one species in a genus is sensitive to that of other species in the same genus, though perhaps not in the same degree. Thus, a person who reacts to pollen of *Quercus rubra* (red oak) is almost certain to react to that of *Q. velutina* (black oak) or of many other oaks.

Hence an idea of the abundance of pollen from a genus is as significant as data on pollen produced by the various species in the genus.

RESULTS OF THE SURVEY

As in other surveys elsewhere, the pollen season was found to fall naturally into four subseasons:

1. The tree season (March-April)
2. The grass season (May-June)
3. The plantain season (June-July)
4. The ragweed season (August-September)

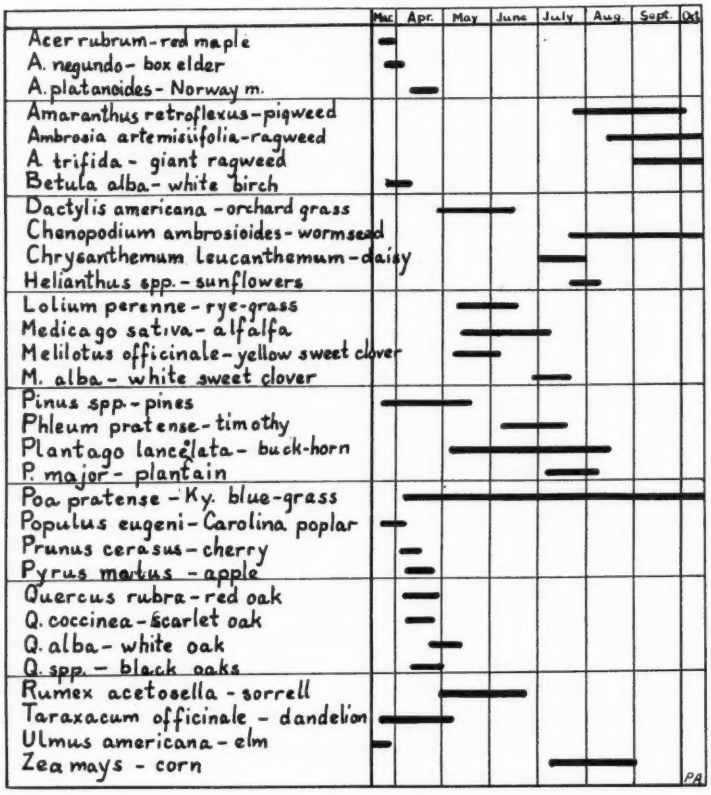

Fig. 3.—Schematic chart of pollen flora, Baltimore, Md., 1929.

THE TREE SEASON, 1929

The tree season began with anthesis of the elms, about March 12, and reached its culmination on April 9, when a total of 700 pollen grains, chiefly from oaks, settled on 1 sq. cm. After this date the number of tree pollens dwindled rapidly, and remained insignificant throughout the rest of the summer. This is to be expected, since almost all northern trees flower before the foliage expands in the spring.

A large healthy tree produces an enormous number of flowers, generally overlooked because they are inconspicuous. Most species of our trees are wind pollinated, hence it is not surprising to find them producing huge quantities of pollen. As a rule the period of pollen dissemination for a given tree species in a locality is short but intense, hence spring hay fever is likely to be of short duration, unless the victim is sensitive to the pollen of a number of different species of trees.

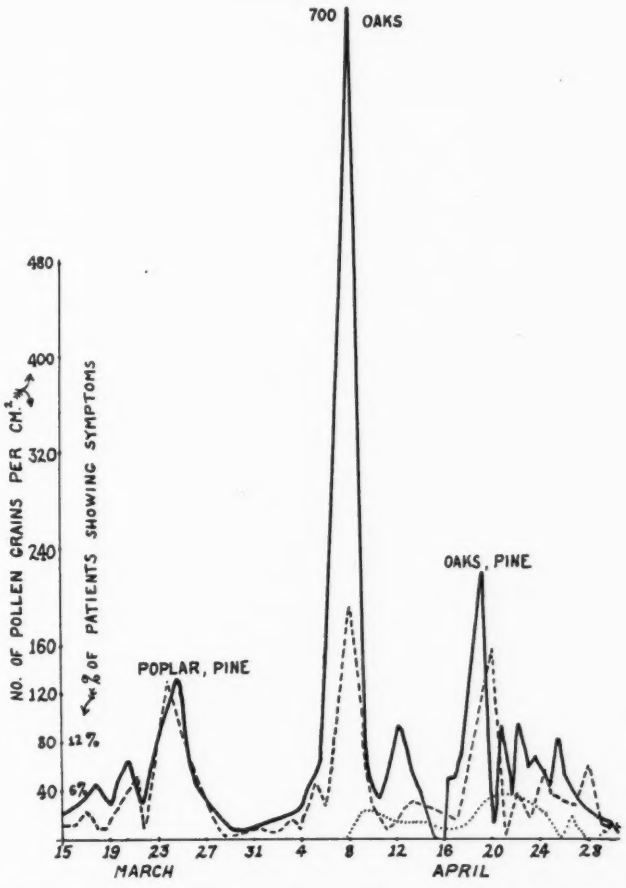

Fig. 4.—The tree season. Continuous line, pollen counts at Station U. Broken line, counts at Station W. Dotted line, percentage of patients showing symptoms of hay fever.

The following species contributed the greatest amount of pollen during the tree season:

Coniferae.—The conifers (pines, spruces, hemlocks, etc.) are not nearly so abundant in middle-eastern latitudes as they are farther to the north (as in northern New England and Canada) in the subarctic soft-wood forests, or farther south in the long-leaf pine districts. Nevertheless, because its extreme lightness enables it to travel farther than any other, coniferous pollen was frequently abundant in

Baltimore. It was found as early as March 1, long before any local conifers were producing pollen. This pollen must have come from the far South, and must have travelled hundreds of miles. Because the pollen obtained had travelled such a long distance from its source it was often difficult to identify it with certainty. Practically all coniferous pollen found in the air, however, was from pine species.

Quercus—the oaks. Red oak pollen was most abundant; that of scarlet oak next, and black oak third. From 10 to 20 per cent of the oak-grains found were recorded simply as from *Quercus* because of the difficulty, discussed above, of making positive specific identifications of oak pollens in all cases. The distinct peak of the oak season occurred on April 8, when 700 oak grains per sq. cm. (chiefly of red oaks and scarlet oaks) were obtained at Station U. The oaks were by far the most prolific source of pollen in Baltimore on any one day during the pollen season of 1929.

Ulmus—the elm. This was the first native pollen appearing on the slides. It first appeared on March 14, at Stations U and W. The season lasted two weeks, reaching maxima of 30 on March 17, and 31 on March 21. Elm pollen was most abundant at Stations U and W. Elms are planted rather sparingly in Baltimore, hence it is not surprising to find its pollen scantily present. In New England cities it is probably much more abundant.

Populus—the poplars. Because of free hybridization among the members of this genus, resulting in intergradation of morphologic types of pollens, it was almost impossible to identify poplar pollen specifically. Most of it seems to come from the Carolina poplars which are planted in great numbers everywhere in Baltimore, except in the most pretentious districts. The poplars produce huge male catkins in enormous numbers, with a correspondingly large amount of pollen. Fortunately, most of this pollen is never shed. Most of the catkins fall and undergo autolytic and bacterial disintegration with most of the anthers unopened. Only a very small fraction of the total pollen produced seems to be liberated. Though Carolina poplars are probably the most numerous trees in Baltimore, the maximum pollen count from them during 1930 was 88 per sq. cm. on March 24. This was at Station W, located about 100 feet to leeward of a long row of huge poplars, which were in full anthesis on that day. The poplar season lasted from March 19 to April 1.

Acer—the maples. Counts on maple pollens were very low. Pollen of red maple (*Acer rubrum*) first appeared on March 20. The total number of grains never exceeded 10 daily, but small numbers, from various species, occurred throughout the tree season. Slides exposed under maple trees, and to leeward of them, showed that maple pollen was not carried more than a few rods by ordinary breezes. Maple flowers showed a large number of abortive anthers, which re-

duced the amount of pollen produced. This may have been an abnormal condition, peculiar to the year. Counts over several years may be necessary to determine this.

Apple and *cherry* pollens were found in considerable numbers on hot spring days. The cherry pollen was found only at Station U. Its source seems to have been "escaped" specimens of the domestic cherry (*Prunus cerasus*) which have grown up in considerable numbers in the wood adjacent to the university campus. The maximum was 41 grains on April 8. None was found after this. Neither the cherry nor the apple pollen seemed to carry well in the wind. Ornamental crab apples and similar plants, of various species and varieties, were the principal source of apple pollens.

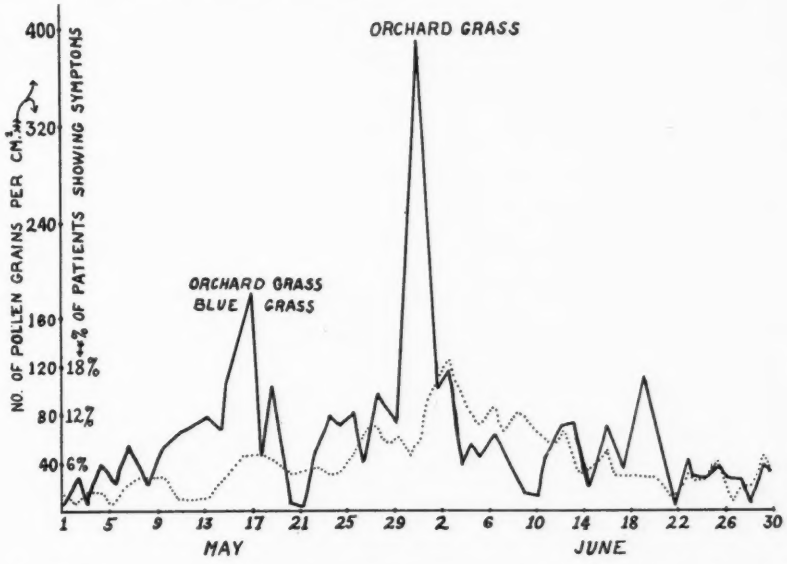

Fig. 5.—The grass season. Continuous line, pollen counts (Station W). Dotted line, percentage of patients showing symptoms.

Betula—birch. Small amounts of birch pollen (usually 10 to 15 grains) were found daily from March 20 to April 10.

Pollens of several other genera of trees and herbaceous plants were found during the tree season, but in such insignificant numbers that little effort was made to identify them positively.

THE GRASS SEASON

The grass season overlaps slightly on the tree season, which ended about May 5. The peak was reached on May 31, with a total of more than 400 grains per sq. cm. These came chiefly from orchard grass (*Dactylis glomerata*). After this there was a rapid decline in grass pollens, and the season ended about June 25.

One grass was far and away the most prolific source of pollen in

Baltimore during this season. This was *Dactylis glomerata*, the orchard grass. It is a large, coarse grass, which grows abundantly by the roadsides and in neglected fields and lots everywhere, and is cultivated to some extent for hay. Its pollen is rather easily recognizable. It is probably the greatest source of grass pollen in the cities of the Middle West and East.

Phleum pratense (timothy) produced only small amounts of pollen during this year. Timothy is one of the most important of cultivated forage grasses, but does not persist, at least in the East, in natural competition with other grasses. Relatively little timothy is cultivated near Baltimore. The maximum count was 25 grains per sq. cm., on June 19. It is usually three to four weeks later than orchard grass. Though it is less common, usually, than orchard grass, more people seem to be sensitive to it than to the latter. Its pollen was found to be very abundant in close proximity to a field of timothy, but it did not seem to be carried far by ordinary winds.

Poa pratensis (June grass, or Kentucky blue grass) produced small amounts of pollen throughout the spring and summer. Seven to 11 or 12 grains were found on each clear day from April 5 to mid-September. The maximum was 37, at Station W, April 8. Blue grass is the most widely used lawn grass everywhere except in the extreme South. The close clipping and mowing to which it is subjected prevents it from flowering abundantly, hence it is not often an important source of pollen, though sensitivity to it may be high.

The following grasses produced small amounts of pollen occasionally during May, June, and July:

Agrostis spp.—bent grass; red top,
Anthoxanthum odoratum—sweet vernal grass,
Avena fatua—oats,
Lolium perenne—rye grass, darnel,
L. multiflorum—Italian rye grass,
Zea mays—corn, maize (July-August).

In the great cereal growing regions of the Middle West, wheat, oat, corn, rye, and other cereal pollens must be abundant at times, but in the East the cereals are not grown in sufficient quantities, especially near the cities, to produce significant amounts of pollen. All species of grasses used locally for hay, however, should be taken into consideration when a patient from rural districts shows allergic symptoms at this time. Hay is commonly cut at or very near the time of anthesis, and the mowing, caring, raking, and stacking may produce very dense local clouds of pollen.

THE PLANTAIN SEASON

This season extending from mid-May to mid-August, overlaps considerably on the grass season. After the main crop of grasses has

flowered, the characteristic early summer plantain season sets in. This is the mildest of the four seasons. Pollen during this season is produced most abundantly by *Plantago lanceolata* (rib grass; buckhorn; English plantain), and in lesser amount by *P. major* (common plantain, pig ear) and *Rumex acetosella* (sheep sorrel).

Other contributors of pollen were:

Melilotus alba—white sweet clover,
M. officinale—yellow sweet clover,
Medicago sativa—alfalfa,
Chrysanthemum leucanthemum—common daisy,
Helianthus annuus—sunflower,
Amaranthus retroflexus—amaranth, pigweed,
Chenopodium ambrosioides—Mexican tea,
C. ambrosioides var. *anthelminticum*—Wormseed,
C. album—lamb's quarters; pigweed,
C. vulvaria—dwarf pigweed (Station W only).

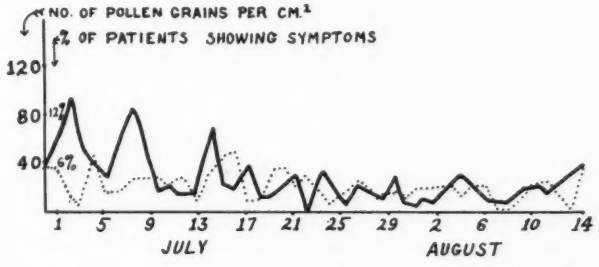

Fig. 6.—The plantain season. Continuous line, pollen counts (Station W). Dotted line, percentage of patients showing symptoms.

No one of these appeared in numbers exceeding 5 or 6 per sq. cm. daily, with a few occasional exceptions.

Rib grass *(Plantago lanceolata)* pollen appeared at a surprisingly constant rate of about 25 grains per sq. cm. daily from mid-May to early August. There were occasional peaks of 40 to 45 per sq. cm. The maximum was 95 grains per sq. cm (Station W) on June 19.

THE RAGWEED SEASON

The first ragweed pollen appeared on August 8. This was from *Ambrosia artemisiifolia*, the common ragweed. Small counts were noted daily, rising rapidly toward the end of the month. On August 28, for instance, the count was 148 grains per sq. cm. at Station W. There was a pronounced drop in the count during the week of September 7 to 14; after this there was a sudden increase, reaching a maximum, for the season, of 205 grains per sq. cm. on September 18, at Station W. Since the other stations gave much lower counts on this date, however, this peak is probably due to some disturbance in the vicinity of Station W,

such as the mowing of weeds in adjacent fields. The significant peak for the season lay in the period from August 26 to September 7. This is reflected in the correlation curve (Fig. 5), in which it is seen that the greatest percentage of patients reported symptoms during this period.

Most of the pollen during the ragweed season came from *Ambrosia artemisiifolia,* the common ragweed. During the latter half of the season there was more or less pollen from *A. trifida*, but at most this never produced more than one-fourth of the daily count. While *A. trifida* is common enough near Baltimore, it is greatly outnumbered by *A. artemisiifolia*, hence these counts are not surprising.

The air during the ragweed season was almost completely free from pollens other than those of the ragweeds, though at this time the

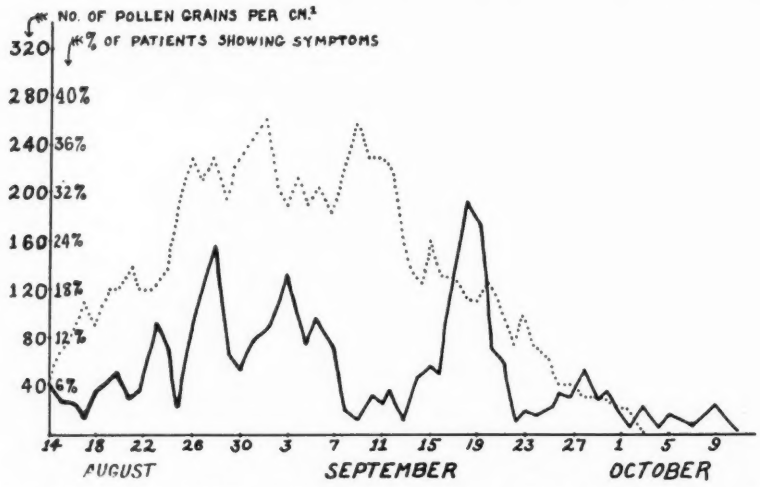

Fig. 7.—The ragweed season. Continuous line, pollen counts (Station W). Dotted line, percentage of patients showing symptoms.

goldenrods, popularly blamed for hay fever, are flowering in enormous abundance. Practically no goldenrod pollen was found on the slides; a few grains from *Solidago canadensis* appeared occasionally, but no others. This is apparently the only common species of goldenrod producing dry pollen. That of other species is sticky, and clots together in masses which could hardly be carried by any wind less moderate than a gale. *S. canadensis* is not so abundant near Baltimore as it is farther north.

After September 20 the pollen counts became low, usually less than 20 per sq. cm. This was still from the ragweeds. These low counts persisted until mid-October, after which no more pollen appeared on the slides.

SPORES

Throughout the entire pollen season spores of different kinds were caught on the slides. The counts occasionally ran as high as 100 per

sq. cm., but were usually from 10 to 30 per sq. cm. These were almost wholly fungus spores, though occasionally a few moss or fern spores appeared. No attempt was made to identify the spores, as this would be a far more difficult task than the identification of pollen grains. A great many of the spores, however (as many as 20 per cent on certain days), were teliospores of rust fungi.

While the number of spores in the air is occasionally high, their relationship to rhinitis and asthma has not been studied sufficiently to warrant an opinion. They are very small—much smaller than pollen grains, as a rule, and are seldom abundant enough, in the open air, to cause continuous seasonal hay fever or other allergic response. Indoors, however, in old damp building, mold or other fungus spores may sometimes be found in great numbers. In barns, damp feed, fodder, old ensilage and decaying fruits and vegetables, may fill the air with spores, and an occasional person may be sensitive enough to these spores to show violent symptoms upon entering such a building.

PLANT HAIRS

Plant hairs are present in the air at all times, winter or summer, and make up a small part of the dust which is settling everywhere. They are sometimes very abundant. During the month of May, hairs from the leaves and inflorescences of various oaks occurred at the rate of 30 to 50 per sq. cm. almost every day. At Station U, situated near several oak woods, the count once rose to 370 per sq. cm. (May 15). The minimum on this day was 103 at Station O. On days like this slides were uniformly coated with a thin white felt, consisting largely of these hairs. Fortunately, the protein content of most plant hairs is very low, probably much less than that of pollens. Nevertheless, because of their occasional sheer abundance, they deserve investigation as possible causes of hay fever and asthma.

LOCAL VARIATIONS IN POLLEN COUNTS

There was considerable variation in the pollen counts of the different stations. Stations U and W, situated in the newer residential districts in the northern part of the city, showed the highest counts, as a rule. The counts at Station U were exceptionally high during the tree season. This is probably due to the proximity of this station to considerable wooded areas. It is also directly to leeward (with respect to the prevailing southwest winds) of a very large park bearing an unusually great number of trees. In both the park and the woods the trees are exceptionally large and luxuriant, and they flower abundantly. Furthermore, the pollen trap was located in a high tower, well above the tops of the trees, where the wind had an unobstructed sweep. The tree pollens were swept out of the tops of the trees and blown along more abundantly at the upper levels than near the ground.

Slides exposed in the Botanical Garden of the University, adjacent to the building which bore the tower, showed smaller counts—usually 30 per cent to 40 per cent lower than those exposed in the tower.

Station W showed decidedly lower counts than Station U during the tree season, but higher counts throughout the rest of the summer. This seemed at first difficult to explain, for while great expanses of weedy fields lie rather near this station, most of them are to the leeward of the prevailing winds. It seems probable, however, that the counts at this station are more typical, for the city as a whole, than those of any other, as is explained below.

The counts at Stations G and O were much alike, though the districts apparently have little in common. Station G, at the plant of the Carr-Lowry Glass Co., near the southwestern edge of the city, lies to leeward of great weedy fields and of broad marshes. From the aspect of the nearby fields one would expect high counts at this station, but they were quite low. This may be ascribed to two reasons: first, the station was in the lee of large adjacent factory buildings, in fact, only direct north or south winds could reach it; second, the many furnaces and ovens of the large glass plant must have maintained more or less constant upward currents of air, especially when the wind velocity was low, preventing pollen from settling. This station, it develops, was therefore not advantageously located. It should have been placed to windward of the plant, instead of in the midst of it. Nevertheless it is interesting to note how slight differences in locale may affect pollen counts. The low counts at Station O, on the roof of the Customhouse, are probably due, in part, to the upward deflection of air currents by the high building. The pollen trap was placed two feet above the roof. Perhaps the counts would have been higher had the trap been placed at the top of the anemometer tower. However, the disparity in counts between this station and Station W is not greater than one might expect to find between the business and the residential sections of a large city. The distance of the business district from the sources of the pollen would have some effect, and the upward deflection of the wind by the tall office buildings must cause a considerable decrease in the rate of settling of the pollen.

Low pollen counts due to the latter cause must be more apparent than real. Slides placed so that they face the wind squarely should show higher counts than those placed edgewise to the wind—a point which apparently has not been considered, but which deserves investigation.

The counts at Station R were astonishingly low, though it is surrounded on all sides by woods and fields which should supply an abundance of pollens of all sorts. The slides were also remarkably free from dust. The only explanation we can offer is that the station was located on rising grounds, in such a way that practically all winds

are deflected upward. Again the low count is perhaps more apparent than real, and would probably be higher with a pollen trap designed to swing with the wind, always presenting the face of the slide squarely to it.

With these criticisms on the location of our stations in mind, the counts at Station W seem the most significant for the following reasons:

1. The neighborhood in which it was located was more nearly typical of the greater area of the city than were any of the others. While East Thirty-third Street (the boulevard on which it was located), is far from being a typical Baltimore street, the adjacent streets, especially those to windward, are characteristically those in which the majority of the population lives. Figures for such an area are surely more important than those for any other.

2. The trap was located at second-story level, within the vertical range occupied by the majority of the population. The count at this level is of more practical importance than that at the top of a high tower, or of a tall office building.

3. There are no adjacent hills or tall buildings to deflect air currents upward, hence the counts are probably more nearly an index of the number present in the air than are counts where upward air currents are keeping pollen grains from settling.

For these reasons, the curves accompanying this article are made from the counts obtained at Station W, unless otherwise indicated.

COMPARISON WITH OTHER SURVEYS

The pollen counts for this region are far below those of the Middle West, as reported by Duke and Durham.[2] Their paper shows high counts wherever surveys have been made in the Middle West, the counts increasing rapidly with decreasing latitude. Duke maintains in this paper that desensitization is much more difficult to obtain, and that it is much more rapidly evanescent in Kansas City, Mo., for example, than it is in Chicago or in eastern cities, because the amount of pollen in the air at Kansas City is much greater than it is in Chicago or in the East. This may be accounted for on the basis of differences of vegetation and of climate. The great plains of the Middle West, with their predominant prairie type of vegetation, bear a high proportion of wind pollinated plants. These always form huge quantities of light, dry pollen. The hot, dry summers of these regions favor the accumulation of great quantities of pollen in the atmosphere. The ragweeds especially seem to thrive in hot, dry summer weather; under these conditions they produce tremendous amounts of pollen. Duke and Durham[2] report for instance, a peak of over 2,000 ragweed pollen grains per sq. cm (7,200 per 0.55 sq. in.) in Oklahoma City in 1926. This is eight times the peak found in Baltimore.

The vegetation of the Atlantic coastal plain tends naturally to establish forest lands rather rapidly, crowding out the heliophilous ragweeds. This restricts them largely to roadsides, vacant city lots, and spasmodically or poorly cultivated fields. The eradication of ragweed, or at least its control by frequent mowing, while at best a Herculean task, would be much more feasible in and near eastern cities than it would be in the southern Middle West. Further, the more even distribution of rainfall which obtains in the East, tends to wash the pollen out of the air, and to keep the counts comparatively low. In midsummer and late summer rains in the Middle West are mostly heavy thundershowers, of short duration and falling over limited areas. As soon as the shower is over, pollen from nearby unwetted regions sweeps in on the wind, so that there is no lasting relief. In the East, on the other hand, rainstorms covering large areas, usually several states, are not infrequent even in mid-summer. These not only wash the air very effectively, but they wash down and beat into the soil any pollen from open flowers of plants. For some hours or even days after such a storm, little pollen gets into the air from the plants, until a large crop of new flowers opens. This means that not only is the actual pollen count kept comparatively low, but there is usually a number of periods of relief for the sensitive person, and these periods are often fairly long in duration.

THE RELATION OF POLLEN COUNTS TO THE INCIDENCE OF HAY FEVER*

The correlation of the incidence of hay fever or other allergic diseases with that of pollen in the atmosphere is important and should prove of general interest. The method of preparing our data was as follows:

One of us (L. N. G.) issued, to each of his patients whom he felt could be relied upon to make the record intelligently, a card upon which could be recorded simply and quickly, the days on which each one showed symptoms of hay fever, mild or severe. Chart 2 shows one of these cards. A total of 67 such cards, completely filled in, were returned in the fall of 1929. The percentage of this group showing symptoms on each day was plotted with the curves made from the pollen counts. (Figs. 4, 5, 6, 7.) These figures show definite correlation between pollen counts and the percentage of patients showing symptoms. It is to be regretted that the number of patients reporting was not larger, but it is large enough to show significantly that the number of hay fever cases varies directly with the pollen counts.

The graphs show that there is some lag—twenty-four to seventy-two hours—between the peaks of the pollen count curve and those in the curve of hay fever incidence. This may be due in part to a delay

*A patient who had symptoms for as short a period as one hour is included in the curves, thus explaining the rather high percentage figures in the spring and summer seasons.

DAILY RECORD OF SYMPTOMS

Name_____ Year_____

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
March																															
April																															
May																															
June																															
July																															
Aug.																															
Sept.																															
Oct.																															

A.

EXPLANATION:

At the end of each day please record the degree of symptoms of hay fever or asthma.

CODE:

Good day	No mark
Poor day	
Hay fever	·
Asthma	⊙
Bad day	
Hay fever	×
Asthma	⊗

By a bad day is meant the occurrence of more or less continuous symptoms.

By a poor day is meant the occurrence of symptoms, morning or evening for from one to two hours.

Total No. Poor Days:—

Total No. Bad Days:—

B.

Chart 2.—*A*, record card; *B*, reverse of card.

between the time of reception of the pollen on the mucosa of the respiratory tract and absorption of a sufficient quantity of toxic proteins by it, but in greater degree to an increasing accumulation of pollen in house dust, which would persist for some time after the outdoor counts had decreased.

There is one glaring discrepancy in the curves for the ragweed season. During the last week in August and the first week in September the counts were continuously high. During the second week in September the counts fell very low, probably because of rain, and during this week the percentage of cases fell rapidly. The percentage

of cases continued to fall, reaching zero on October 3, but the highest peak in the pollen counts for the ragweed season came on September 18. The counts rose rapidly and fell again as rapidly, but there was very little increase in the number of patients reporting symptoms. This is difficult to understand, but these factors may help to explain it:

(1) Most of the patients had been receiving treatment throughout the season, which was probably becoming increasingly effective by this time.

(2) The peak, although high, is narrow, lasting only four or five days, and reaching its height on only two days. Moderately high counts over a period of a week or more seem to be more effective in producing allergic reactions than high counts during a short period. A comparison of the peaks in the tree and grass season with those in the ragweed season bears this out.

(3) The high peak was found only at Station W. At the other stations the increase in counts in this week were not so great. The high peak at Station W may have been due to a change in wind direction lasting several days, or to a local disturbance, such as mowing of weeds in nearby fields.

The curves also show a commonly observed feature: that by far the greatest percentage of cases of hay fever is reported during the ragweed season. The following are possible explanations of this:

1. There seems little doubt that ragweed pollens are more potent than any others. They affect a greater number of people and give more violent reactions than other common pollens.

2. Ragweed pollens are produced in uniformly high numbers through a period of long duration—two to four weeks—and as mentioned above, this long period has as much significance as have high counts, perhaps more. It gives time for sensitization or resensitization, followed in some days by allergic response to further inhalation of the same pollens. The combination of this factor and the previous one makes the ragweed season the one of most prolonged and most intense misery to the hay fever victim.

3. The comparatively short duration of high counts in the tree and grass season decreases the number of patients feeling symptoms.

4. Perhaps a large percentage of spring and early summer hay fever and asthma, especially the milder cases, is never reported as such, but dismissed as bothersome but quickly passing "spring colds," not worth bringing to a physician's attention. While it would be difficult to obtain any exact information on this point, it seems probable that a great percentage of the sniffling and sneezing observable in April and May and perhaps part of June is allergic rhinitis due to pollens, and not coryza. It is usually mild, and comes at a time when colds are expected by the populace, hence is overlooked.

SUMMARY

1. Pollen counts indicate that the pollen season in Baltimore, as elsewhere, falls into four subseasons: the tree season (April and May); the grass season (May and June); the plantain season (June, July, early August); and the ragweed season (mid-August to mid-September).

2. The highest counts occurred in the tree season, second highest in the grass season, and lowest in the plantain season.

3. The counts in the ragweed season, while lower than the maxima of the tree and grass seasons, are uniformly high over a period of nearly a month.

4. Pollen counts were low compared to those obtained by other workers in the central and southern Middle West.

5. A definite and direct correlation was found to exist between pollen counts and the incidence of hay fever and asthma in a moderately large group of patients under observation throughout the pollen seasons.

The authors take this opportunity to thank Mr. Roscoe Nunn, director of the Baltimore Station, U. S. Weather Bureau, and Mr. W. Leach, the manager of the Carr-Lowry Glass Co., for their kindness and cooperation in establishing and maintaining these stations.

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THE INFLUENCE OF ADRENALIN UPON THE VITAL CAPACITY IN ASTHMA*

Preliminary Report

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Boston, Mass.

THE purpose of this study was to determine the influence of adrenalin on the vital capacity in asthma. There is but meager reference in the literature on the subject. In 1925 Seeley Mudd[1] studied three cases of asthma and found that their vital capacities increased 20 per cent, 71 per cent, and 100 per cent respectively after the subcutaneous injection of adrenalin chloride. Obviously this number is too small from which to draw final conclusions, and so it seemed to us worth while to repeat these observations on a larger scale.

Since variations in vital capacity readings often arise in the same patient due to improper technic, we tried to eliminate this by training our patients in spirometry in the course of weeks at each visit to the hospital or office. Subsequently, the observations were made on those patients who presented themselves for examination with symptoms of dyspnea and wheezing, indicating the presence of bronchospasm at that time.

Type of Patient.—Twenty-seven patients were studied; 15 males and 12 females. Their ages ranged from twelve to seventy-nine years.

Type of Asthma.—The duration of the disease in this group ranged from one week to forty years. In all but three cases the asthma was perennial, although periods of freedom from symptoms at various times and for various intervals were noted in every instance. Clinically, these patients could be placed in the group of "infected asthmas," since all but three gave evidence of a coexisting bronchial infection in addition to the bronchospasm. In the three instances where the asthma had lasted only one week, two months, and four months respectively, there was only suggestive evidence of bacterial infection. Furthermore, the short duration of the disease, in these three cases, precluded the possibility of fixed changes in the mucosa and muscularis of their bronchi, a factor which could possibly influence the effect of adrenalin on the vital capacity in the rest of the group.

*From the Anaphylaxis Clinic of the Beth Israel Hospital, Boston, Mass.
From the Anaphylaxis Clinic of the Massachusetts General Hospital, Boston.
Read before the Seventh Annual Meeting of the Society for the Study of Asthma and Allied Conditions, Atlantic City, May 2, 1931.

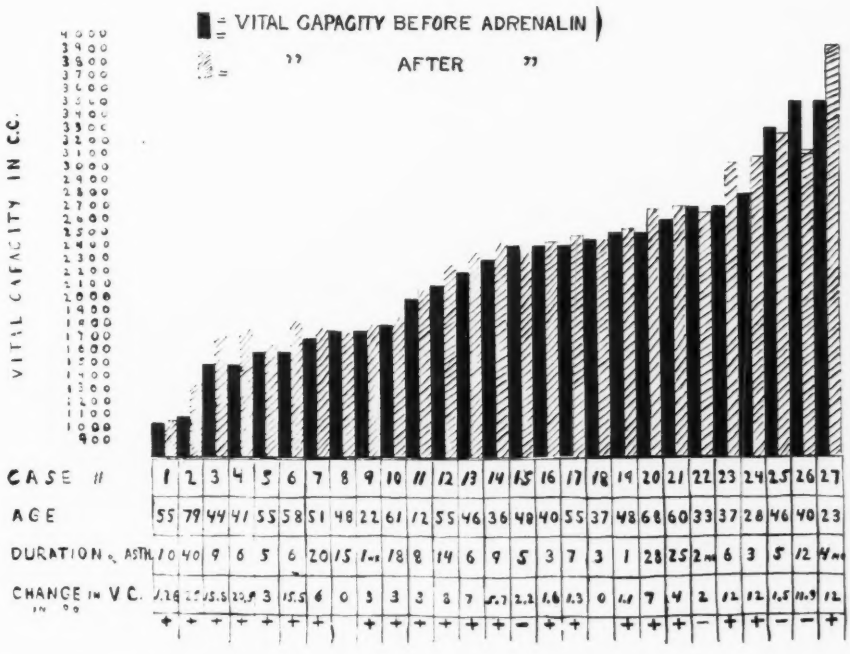
Particular attention was paid to the heart in this group in order to eliminate cardiac weakness as a factor in the patient's dyspnea. This was accomplished by physical examination in addition to x-rays and electrocardiograph tracings, where indicated.

Technic of Experiment.—In carrying out the experiment the patients were submitted to the following procedure:

After a period of rest from twenty to thirty minutes the vital capacity was recorded. Then 0.5 c.c. of adrenalin chloride 1-1000 was injected subcutaneously. Vital capacities were subsequently read after

CHART I.

THE INFLUENCE OF ADRENALIN ON THE VITAL CAPACITY IN ASTHMA



five, ten, fifteen, and thirty minutes. The average for the four readings was estimated and compared with the pre-adrenalin readings.

The results were as follows: In four patients there was an actual decrease in vital capacity 1.5 per cent, 2 per cent, 2.2 per cent, and 11.3 per cent respectively, all of which must be attributed either to faulty technic or lack of cooperation on the part of the patients. In two patients there was no change either way. In nine patients the increase was from 1 to 5 per cent; in six patients from 5 to 10 per cent; in three patients from 10 to 15 per cent; in two patients from 15 to 20 per cent; and in two patients from 20 to 25 per cent.

In Chart 1 the patients are arranged according to their initial vital

capacities of which the solid black column is representative. The hatched column on the right represents the vital capacities after adrenalin. At the bottom of the chart the number and age of the patient, the duration of the disease, and the results of the observations in percentages are posted.

We observe from this chart that in this group of patients neither age nor duration of the disease influenced the effect of adrenalin on the vital capacity. Thus in Case 11, where the patient's age is twelve years, the increase in vital capacity is 3 per cent, while in Case 2, where the age of the patient is seventy-nine years, the increase in vital capacity is 25 per cent, the contrary of which might have been expected. Again in Case 10, where the asthma is of thirteen years' duration, the increase is 3 per cent, which is the same as in Case 9 where the asthma is of one week's duration. These results are striking when we note that in Cases 9, 22, and 27, where bacterial infection is not a complicating factor, the final results are no different than in the rest of the group.

Particularly interesting is the patient in Case 27, who upon first examination in the office, when free from asthma, had a vital capacity of 4,400. On another occasion, however, when he came in choked with asthma, his vital capacity was only 3,300. While adrenalin raised his vital capacity to 3,800, it failed to bring it up to its normal height of 4,400 as previously observed.

Several other such instances could be quoted where patients were seen while feeling well and at a time when their vital capacities were much higher than the readings obtained after adrenalin administration in an attack.

What impresses us most in these observations is the fact that all patients felt relief from dyspnea after they had received a dose of adrenalin, notwithstanding the fact that the change in vital capacity was not always in their favor. This relief can be explained on the grounds that it is not real dyspnea that dominates the asthmatic attack, but distress which is due to the tetany of the bronchial musculature. Upon the relaxation of this tetany by adrenalin the patients' symptoms are ameliorated. On the other hand, the failure of the vital capacity to increase materially after adrenalin administration must be attributed to the persistence of the mucosal edema and possibly the presence of some secretion in the bronchial tubes which are important component factors in the asthmatic attack.

By analogy, we observe the events in angioneurotic edema where patients experience relief from itching after the administration of adrenalin before the blotches or edema on the skin disappear.

We cannot avoid calling attention to the impression of the low initial vital capacities in asthma, although this point has been re-

peatedly emphasized by other observers.[2, 3, 4] It is clear, however, that the height of the initial vital capacity bears no relationship to its rise after adrenalin administration. Thus we see in Case 2 an initial vital capacity of 1,000 with a rise of 25 per cent after adrenalin administration, while in Case 27 where the initial vital capacity is 3,300, the final reading shows a rise of only 11 per cent.

SUMMARY

1. The effect of adrenalin upon the vital capacity in asthma has been studied in a group of 27 cases, 24 of whom suffered from infected asthma, while in three cases infection was not an important factor in the disease.

2. The results indicate that irrespective of the type of asthma, the increase in vital capacity may be slight or none at all after the subcutaneous injection of adrenalin.

3. The relief experienced by all patients after the administration of adrenalin can be attributed to the relaxation of the bronchial tetany which seems to be responsible for the patient's distress.

4. The failure of the vital capacity to increase appreciably after the administration of adrenalin can be explained by the persistence of the mucosal edema and hypersecretion of its glands which may interfere with lung ventilation.

5. In this group of patients neither age, duration of the disease, nor the height of the initial vital capacity bore any relationship to the change in vital capacity after adrenalin administration.

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BLOOD PRESSURE IN ALLERGIC INDIVIDUALS*

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IN A BUSY clinic, as the clinician interviews and examines patients, he is impressed with certain findings, which soon become facts in his mind, only to be disproved by a later statistical study. As an example I might cite one such idea, that the shorter the duration of asthma, the better the results, which was disproved by Clarke, when he showed the poor results in patients seen early in the course of the disease, a study which he offered as a manifestation that asthma is a self-limited disease.

The present study was undertaken to present some facts in confirmation of ideas obtained in routine clinic work with patients in our asthma department, and this time the impressions and facts coincided to some degree. I refer to our opinion that hypersensitive individuals as a rule have blood pressures below average values. This impression was so well fixed in our minds, that in one instance a foreign-born patient from whom no description of his complaint was obtainable, and in whom physical examination was negative; a blood pressure below the average influenced his further study, which revealed skin-test evidence of early hay fever.

Whether other observers are in accord with our opinion, it is difficult to determine from the literature. Rackemann,[1] Sihle,[2] and Alexander, Luten and Kountz,[3] noted a fall in blood pressure during a paroxysm, which was attributed to an increased intrathoracic pressure. Alexander, Luten and Kountz, further state that individuals with asthma tend to have blood pressures below the average for comparative ages, quoting an average blood pressure of 118/74 for an average age of thirty-nine years in a series of 50 cases.

TABLE I

SYSTOLIC BLOOD PRESSURES IN ALLERGIC INDIVIDUALS

AGE IN YEARS	SYSTOLIC BLOOD PRESSURES								NUMBER OF PATIENTS
	80-100	110	120	130	140	150	160-200	200+	
15 to 30	31	50	86	26	17	2	4	0	216
30 to 40	31	46	66	53	16	8	15	3	238
40 to 50	20	36	57	24	31	12	20	5	205
50 to 60	12	19	20	18	21	21	26	5	142
60+	6	3	11	10	17	8	20	5	80

*Read before the Seventh Annual Meeting of the Society for the Study of Asthma and Allied Conditions, Atlantic City, N. J., May 2, 1931.

In the present study we have grouped the number of patients in the different age groups, as shown in Table I, in columns headed by their range of systolic blood pressures estimated in millimeters of mercury. Herein one may observe in a comprehensive way the tendency toward lower values. Note, the large number of patients, even up to fifty years of age, with systolic blood pressures of 110 or less. One hundred and thirty-three of 443 patients between thirty and fifty years had systolic pressures of 110 or less. Seventy-one of 222 patients over fifty years had pressures below 120. The number of patients is shown in the last column.

TABLE II

COMPARISON OF BLOOD PRESSURES BETWEEN NORMAL AND ALLERGIC INDIVIDUALS

AGE	AVERAGE NORMALS (SYSTOLIC)	PATIENTS WITH ALLERGY	HYPERTENSION EXCLUDED
15 to 30 years	123	118 / 77	109 / 77
30 to 40 years	126	124 / 82	119 / 79
40 to 50 years	128	129 / 84	120 / 79
50 to 60 years	133	138 / 87	121 / 81
60 years	138	141 / 84	125 / 79

In table II, the normal average systolic blood pressure is compared, in the comparative age groups, with average pressures of 881 allergic patients, including those with definite cardiovascular disease and hypertension. The normal averages are from the table of Warfield,[4] who presents it from a series of published figures of blood pressure observations, with the diastolic pressures stated as 70 to 85 per cent of the systolic pressures. The normal and allergic pressures in the first two columns show little difference. The gross average for all normals is 129.6 and for all allergic patients 130 mm. of mercury. The latter group shows lower values up to forty years with greater pressures after that age. The reason for this increase brings us to the consideration of those patients with hypertension, who present themselves for treatment of their dyspnea. Physical examination excludes some, but it is impossible to decide accurately when all the symptoms are due entirely to hypertension and when allergy coexists.

Since allergy does not warrant immunity to the other ills of mankind, diabetes perhaps excepted, we believe that those patients with hypertension complicating their allergy should be excluded when we try to estimate the average blood pressure for the atopic individual. Excluding all patients with a systolic blood pressure of 150 or over,

we have presented in the third column the blood pressures for uncomplicated allergic patients. The values here shown are consistently below those for normal individuals. The gross average is 119/79. I believe these figures represent the truer measure of the average blood pressure in allergy. A tendency to lower diastolic pressure in the older age groups was also noted.

Of the 881 patients, 103 showed systolic pressures above 150. Over half of the hypertension patients were more than fifty years of age and gave an average pressure of 178/105. Eighty-eight of these hypertension patients were studied in some detail with regard to their asthma and result of treatment. The average period of observation was one and one-half years, while the average duration of the disease was eleven years. Seventy-two or nearly 90 per cent were diagnosed asthma chiefly on the physical signs in the chest; one case on the finding of eosinophils in the sputum. Only eight of 38 patients showed a definite nephritis with albumin and casts. Seventeen of 57 showed enlargement of heart on x-ray examination. Two-thirds of the patients had definite evidence of foci of infection. Fifty-five per cent or 49 patients gave positive skin tests.

Treatment of this hypertension group of patients, was the routine treatment of asthma, removal of offending specific causes where possible and specific injections when indicated. All foci of infection were treated or removed. Where no specific hypersensitiveness was demonstrated, injection of stock vaccine was used. The usual drugs —potassium iodide, ephedrine and adrenalin for attacks—constituted the rest of the treatment. Injections of adrenalin for acute attacks are not contraindicated in the presence of high systolic pressures. It has been observed repeatedly that such injections in acute attacks of asthma lower the pressure from ten to twenty points in less than ten minutes. In Table III, the results are tabulated and compared with the results obtained in the entire series reported by Clarke[5] in 1927. Fifty-nine and two-tenths per cent gave unsatisfactory results, while 40.6 per cent were satisfactory. Only 8.4 per cent were almost completely relieved.

TABLE III

COMPARISON OF RESULTS OF TREATMENT OF PATIENTS WITH HYPERTENSION AND ASTHMA TO ENTIRE SERIES

	ENTIRE SERIES	HYPERTENSION AND ASTHMA
0	14.5%	23.4%
+	23.0%	35.8%
++	41.7%	32.2%
+++	20.8%	8.4%
Number of cases	882	81

0, + = unsatisfactory results.
++, +++ = satisfactory results.

In taking the blood pressure readings, no attempt was made to obtain the minimum pressure. The readings were taken during the routine physical examination, usually on the first visit to the clinic.

CONCLUSIONS

1. The average systolic blood pressure of 881 allergic patients was found to be 130. Excluding those with pressures 150 or over (definite hypertension) the average was 119.

2. Unusually low figures were obtained in those over fifty years of age who were normal except for the asthma—71 having pressures of less than 120 systolic.

3. When hypertension and asthma coexist, the prognosis of the asthma is poorer than in the nonhypertension patient.

4. Strongly positive skin reactions are seen in those with well-marked hypertension.

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(For discussion, see page 400.)

STUDIES IN ASTHMA: XII

The Plant Pollens of New England. Their Relative Importance*

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and
Lyman B. Smith, Ph.D.
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POLLEN surveys are always important to the study and treatment of hay fever. An accurate knowledge of the time periods during which the pollen of different plants is thrown off into the air would be valuable, but real accuracy is quite impossible because the seasons vary so widely in the different years. In New England, pollen surveys have been made by Mr. F. H. Hodgson working with Vander Veer, Cooke, and Spain[1] in 1924-1925 and more recently by one of us[2] working at the Gray Herbarium of Harvard University.

Chart 1 represents the preliminary survey. The heavy horizontal lines show for each plant the period of active pollen production while the dotted extensions indicate the sporadic flowering which occurs after the true season has ended. This chart is compiled in its early part from the specimens in the collection of the New England Botanical Club, and the lines, therefore, represent the extremes of pollen production for many years rather than the production in any one year. The last part of the chart, from June 15 on, represents the field and air observations of 1930. These, however, have been found recently to check fairly well with the herbarium collection, and it is our belief that variations in different years are much more marked in the early than in the late season.

When our chart is compared with the chart of Hodgson, there are occasional discrepancies though none of them are marked. For example, low spear grass *(Poa annua)* flowers in New England throughout the frost-free months. Its field incidence, however, is relatively infrequent. Elm is indicated with a season from April 10 to 30—a total of twenty days. Chart 2, however, shows that this year (1931) the season during which elm pollinated extensively was only six days long (April 9-15). In passing, it is most interesting to observe that during this short period the concentration of elm pollen found on slides in two different locations reached a figure of 200 grains which is twice the maximum concentration (100) observed in September, 1930, for ragweed. This illustrates very well the discrepancies in all surveys.

*From the Anaphylactic Clinic of the Massachusetts General Hospital and the Gray Herbarium of Harvard University.

Read before the Seventh Annual Meeting of the Society for the Study of Asthma and Allied Conditions, Atlantic City, N. J., May 2, 1931.

The expenses of this investigation were met by an anonymous donation known as the "M. G. H. Asthma Fund."

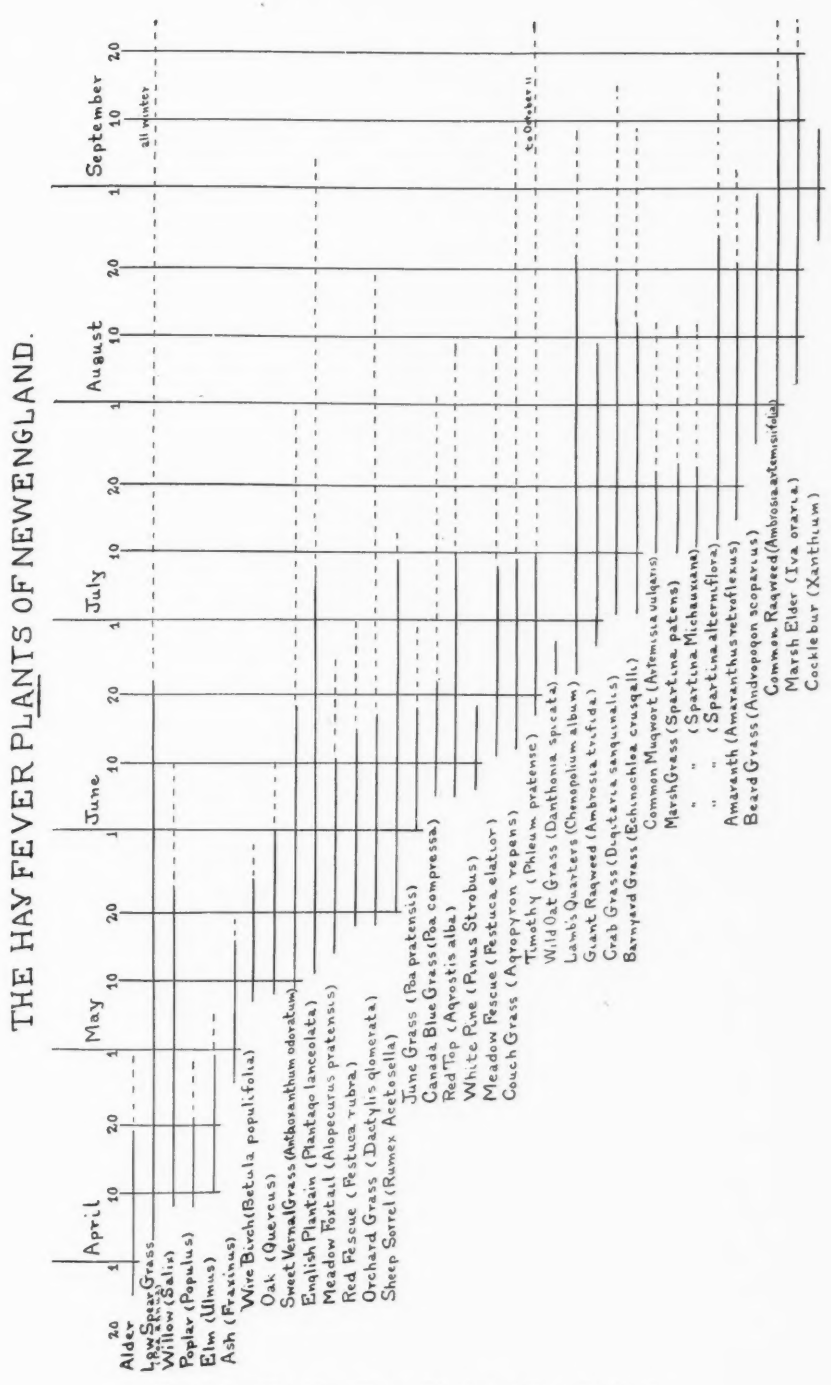

Chart 1.—The Hay Fever Plants of New England.

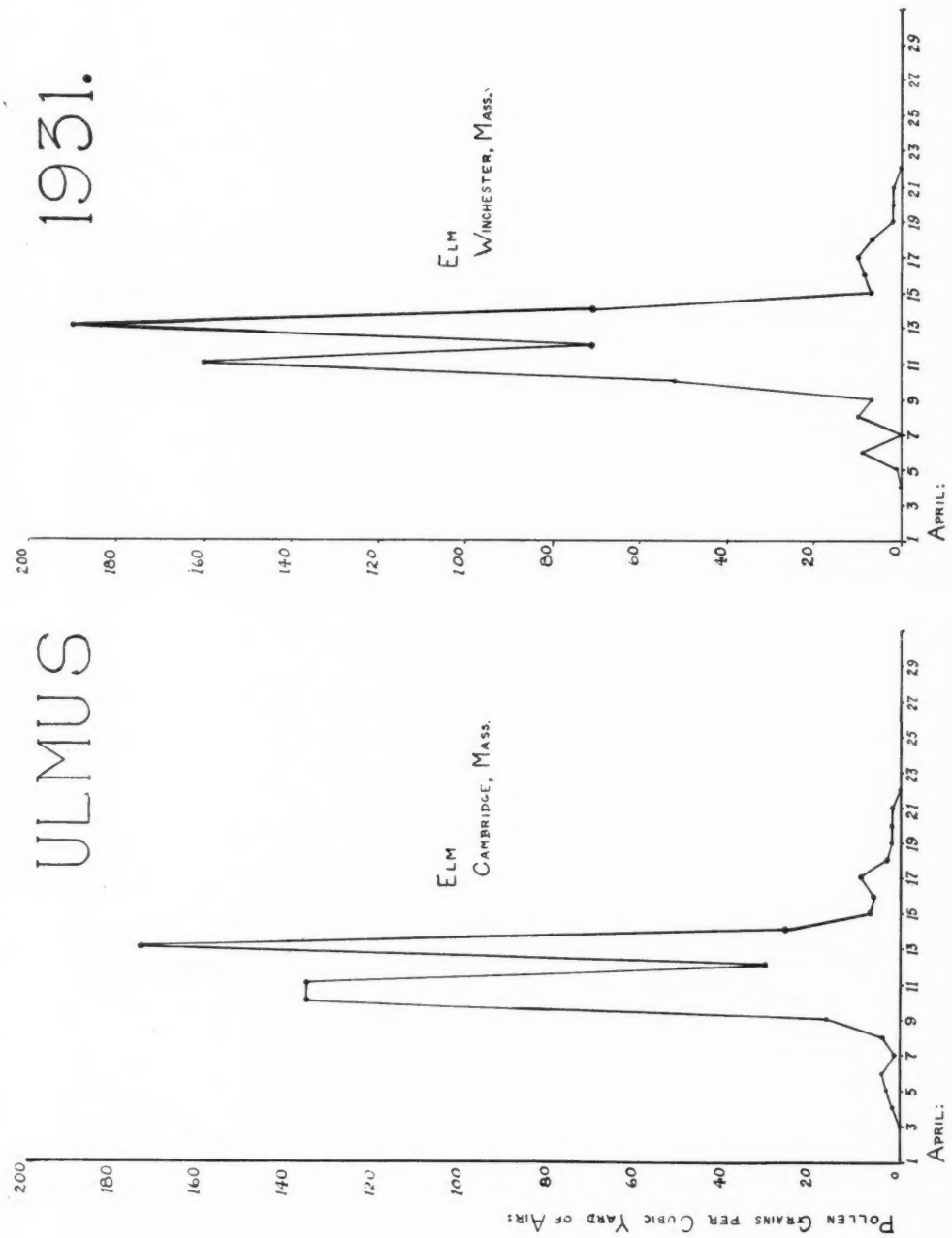

Chart 2.—Elm Pollen 1931. Pollen counts per cubic yard of air observed in Cambridge and Winchester, Mass. Note that the real pollen shed lasts only six days and is quite the same in two locations 8 miles apart.

As said, these discrepancies are much more evident in the early season and apply particularly to the trees.

Sweet vernal grass which blossoms in early May may continue past the fourth of July. English plantain likewise appears early in May and continues as an active pollen producer until well into July and perhaps August. Orchard grass also comes early. It may appear in the middle of May although Hodgson did not find it until after the first of June. It also may continue into August. Orchard grass blooms about two weeks before June grass and red top, the latter two being intermediate between orchard grass and timothy. Timothy appears some time between the middle and end of June and may persist sporadically throughout the summer into October. Lamb's-quarters, crab grass and giant ragweed (which last is rare in New England) may all pollinate in late June but may all continue to blossom into September. Lamb's-quarters is a very common weed but our skin tests with the pollen are mostly negative. Apparently, it is not an important factor in any number of cases.

It is unusual for hay fever patients to begin their symptoms in early July, that is, in the intermediate period between the grass season and the ragweed. The plants listed here are relatively unimportant for various reasons. Some like meadow foxtail, fescue, giant ragweed, artemisia, and cocklebur are never found in stands large enough to be significant; while others like marsh grass and marsh elder do occur in large stands but these are restricted to localities where they have slight opportunity to be effective. In another group are such plants as wild oat grass, lamb's-quarters, crab grass, barnyard grass, amaranth and beard grass which are relatively common and well distributed but which appear to be very poor pollen producers in this region.

The lists of plants presented by Hodgson and by ourselves are not the same. Each includes plants which are not given by the other perhaps because these plants were more impressive in one locality than another.

What do these different findings mean? Theoretically, the treatment of hay fever should be highly specific. While Chobot[3] has shown that there is a considerable immunologic overlapping between the pollen of one grass and another, we believe that the question of a specificity is still an open one.

Chart 3 shows the symptoms suffered by 100 patients who were treated with ragweed in 1930. The duration and severity of the symptoms are shown by the horizontal lines, each of which represents the experiences of a single patient. Counts have been made of the number of cases showing symptoms on each particular day, allowing two counts for the heavy lines which indicate severe symptoms. From these counts, the heavy black curve has been constructed. It cor-

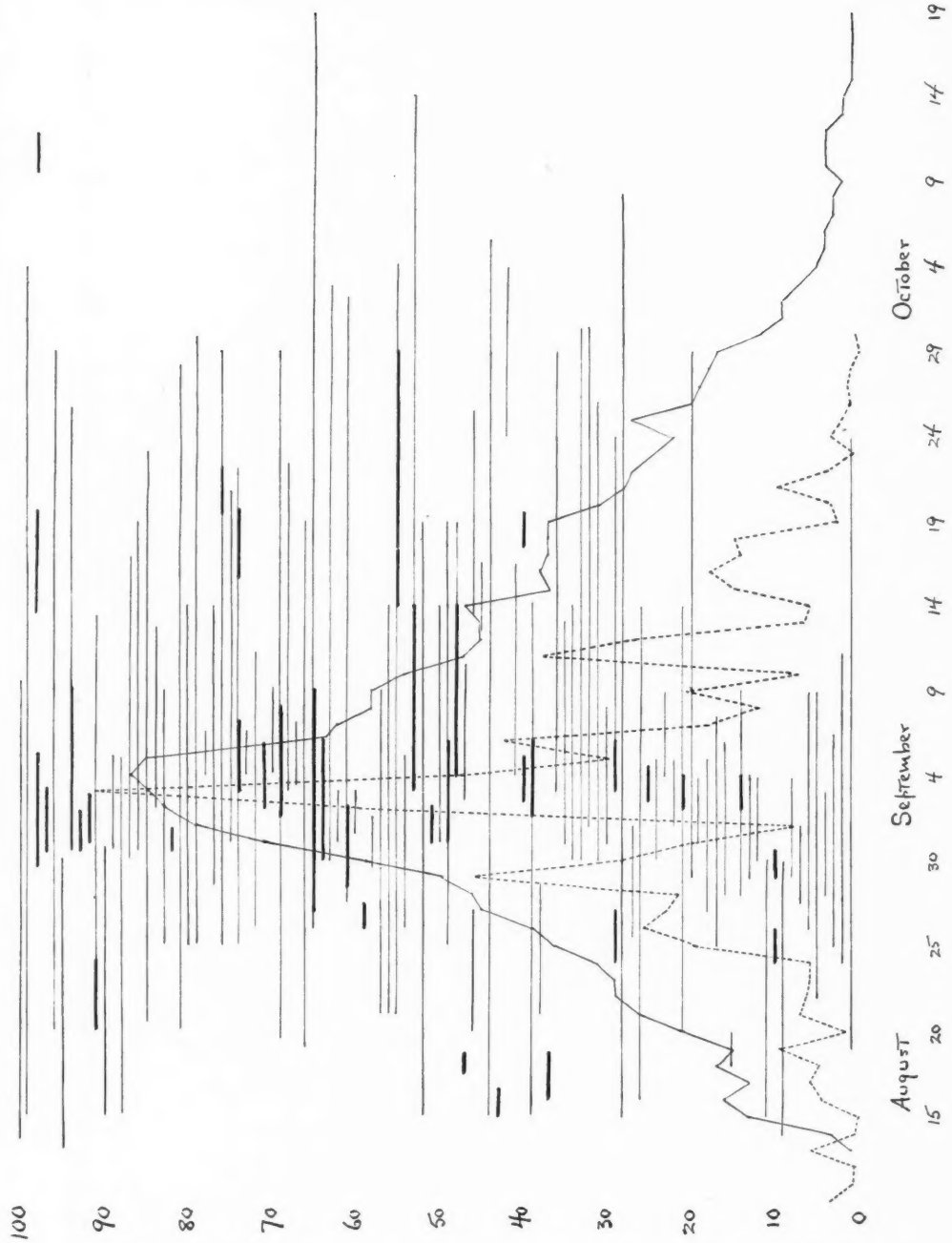

Chart 3.—Ragweed hay fever. Symptoms and pollen concentration compared, 1930. Horizontal lines indicate symptoms in each of 100 cases. Dotted curve shows pollen grains per cubic yard of air.

responds very well to the dotted curve which was made quite independently by Dr. Smith and which represents the concentration of ragweed in the air. The close similarity of these two curves indicates that in the case of late hay fever, the symptoms must depend upon one particular plant—ragweed.

Chart 4 is constructed in the same way. It shows the symptoms in 100 cases of grass hay fever treated in 1930. Here the composite curve of symptoms covers a much longer time period and is only half as high. In many cases the individual lines are long, indicating that the symptoms persisted for many weeks and suggesting that the patient is sensitive to a variety of grasses. Incidentally these prolonged symptoms were usually mild. They were often limited to a fit of sneezing in the early morning. Severe symptoms indicated by the heavy lines were observed in only 7 per cent of the grass cases in contrast to their occurrence in 30 per cent of the ragweed cases (see also Chart 3). In the grass group, these severe symptoms did not occur at the same time in all the cases. Where the symptoms were of brief duration and the line was short, this line appears sometimes in June and sometimes in late Juy. Obviously, there is much less uniformity than in the ragweed series.

These observations indicate, we believe, that different patients are sensitive to different grasses; that one grass is the primary factor in one case and another grass in another case. The long low curve of total symptoms in the whole group is due to the fact that the grass seasons overlap to a considerable extent. In four cases, the symptoms continue into August—each of the four reacted to plantain as well as to the grasses.

On the other hand, the question of multiple sensitiveness to several different grasses at the same time finds support in the fact that almost every one of the grass patients reacts by skin test to almost every one of the grasses and to each grass in about the same degree. The multiplicity of reactions occurs quite regardless of whether the symptoms are early or late in the grass season. Since we have learned, however, that positive skin tests can frequently occur without evidence of clinical sensitiveness, it seems to us that many of these positive grass tests can be neglected.

Our practice, therefore, is to select for use in treatment those pollens which correspond in their time of pollination with the times during which the patient has symptoms, provided of course that he gives positive skin tests to them. In making the selection, a copy of our survey is always before us. Thus, if the symptoms begin in May, the pollen of sweet vernal grass, of plantain, and of orchard grass, sometimes one alone, sometimes two at a time, are selected for use in treatment. If the symptoms begin in early June, June grass or red top is considered, whereas later in June, timothy is the choice. Couch grass

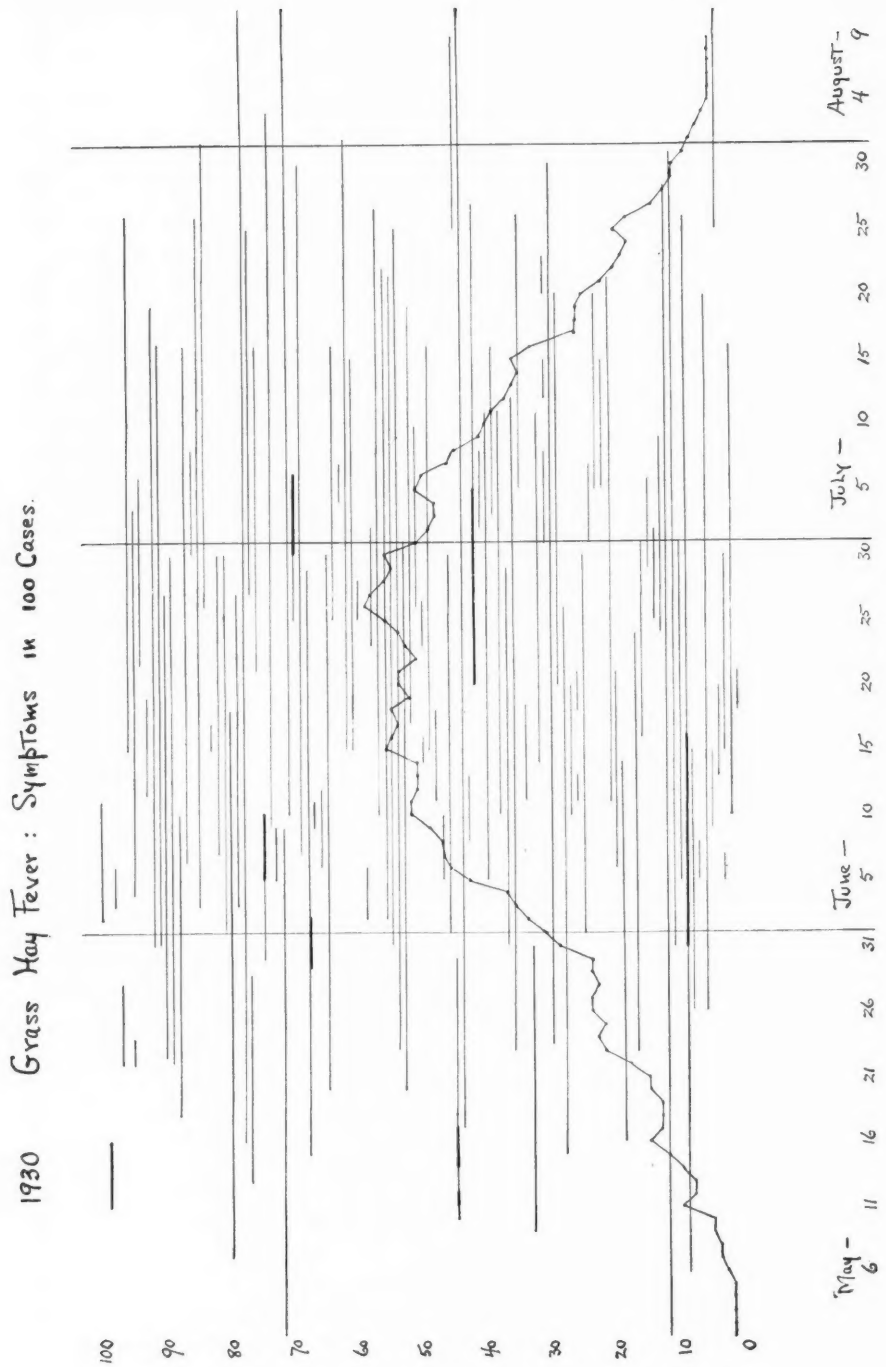

Chart 4.—Grass hay fever. Symptoms in 100 cases 1930. The horizontal line shows the symptoms for one patient.

(*Agropyron repens*) is common near Boston. Extracts of its pollen give positive skin tests in most of our grass cases, and as its season of pollen production closely parallels that of timothy, we are using couch grass in the treatment of several cases.

CONCLUSIONS

1. A preliminary survey of the hay fever plants of New England is demonstrated with a discussion of its limitations.

2. In the case of late hay fever, symptoms correspond closely to the concentration of ragweed pollen in the air.

3. In the grass cases, the lack of uniformity in the occurrence of mild or of severe symptoms indicates that different patients are sensitive to different grasses even though the long season in some cases and the finding of positive skin tests to several different grasses at the same time suggests a multiple grass sensitiveness.

4. We believe that the selection of grass pollens for use in treatment should be determined by the time of symptoms as indicated by pollen surveys.

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(For discussion, see page 392.)

LOCAL PASSIVE TRANSFER TO A FREQUENTLY RECOVERED STRAIN OF STAPHYLOCOCCUS HEMOLYTICUS CASE REPORT*

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With the Assistance of
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Toronto, Canada

MRS. B. M. B., aged forty years, was seen in consultation September 24, 1928, as a suspect tuberculosis on account of hemoptyses and irregular temperature, the maximum being 104° F. with irregular and sudden returns to normal.

The previous history was voluminous and included an enormous mass of symptomatic detail with almost constant medical attention for years in England (which she left at the age of seventeen years), the United States, and Canada. In this almost wild array of symptoms those referable to the gastrointestinal system were predominant. The thyroid had been removed some years before and as well the appendix and pelvic contents.

Physical examination was negative in regard to the chest, and stereograms indicated no evidence of tuberculosis. Time and repeat examinations have excluded any possibility of tuberculosis: and, though repeated small hemoptyses have occurred, no evidence has ever been found of any persistent pathologic lesion of the upper or lower respiratory tract. Gastrointestinal examinations have excluded ulcer, cancer, or any other demonstrable condition.

Certain of her rather indefinite statements regarding the suddenness of her gastric pain led me to suspect she was allergic.

In June, 1929, a number of tests, both scratch and intradermal, showed marked reactions to certain of the autumn pollens especially ragweed and a few of the foods. During the course of preseasonal pollen desensitization she complained of what she called a pharyngitis which I learned was often associated with or followed by intense abdominal pains and occasional dysentery.

A culture from the throat at this time showed only a hemolytic staphylococcus to which on both scratch and later intradermal tests she gave large wheal reactions with surrounding areolas.

The increase of pollen solution was achieved with great difficulty—frequently second decimal point increases only. The reactions were

*From the Christie St. Hospital, Toronto, Canada.
Read before the Seventh Annual Meeting of the Society for the Study of Asthma and Allied Conditions, Atlantic City, May 2, 1931.

peculiar in that at first they would be intense areolas with subsequent hemorrhagic ecchymosis, flushing of the face with perspiration and tremor. It was found at this time impossible to incorporate the autogenous vaccine on account of the reactions.

During February, 1930, this vaccine diluted one hundredfold was given by her own physician with a resulting general anaphylactic reaction of extreme severity.

The following is an attempt to summarize the results we have obtained regarding sensitization to this strain of staphylococcus which has been recovered in pure or mixed cultures with other varieties on all four occasions during a self-labelled "throat attack."

On October 13, 1930, scratch and intradermal tests were made with twelve different strains (in dilute suspension) of staphylococcus and streptococcus including three of those recovered previously. To the three autogenous strains and one other, areolas measuring up to 15 mm. were obtained. On October 19 she had an attack of severe gastric pain and two of her own recovered strains reinflamed forming wheals which broke down. I should add that the tested areas had completely recovered and were barely visible.

A somewhat similar experience had been previously observed with regard to food tests, which had been done on June 2, 1930. On August 15 she broke away from her prescribed diet with reflaming of the tests which were positive on June 2.

In view of the facts (1) that typical reactions had been obtained with her autogenous strain, (2) that a severe general anaphylactic reaction had been obtained by the use of this as a vaccine, and (3) that reflaring of old tests to both food and cultures had taken place during spontaneous attacks, it seemed worth while attempting local passive transfer.

This was first attempted on August 15, 1930, when 0.1 c.c. serum diluted 1-10 was injected intradermally in five areas in two known receptors. On August 16 these areas were reinjected with ragweed solution (to which the patient was sensitive), to the autogenous culture recovered in 1929, to the autogenous culture recovered in 1930, and to June grass to which the patient was not sensitive, the fifth serum area being left as control.

Wheals began to form almost immediately to the ragweed areas and to both the culture areas, while June grass and the serum control remained negative; the only difference between the ragweed areas and the culture areas being that the pollen reaction came on more rapidly but the culture reactions persisted longer. The maximum areola with the ragweed was a 50 × 60 mm. areola in thirty minutes, the maximum reaction to the bacterial emulsion being 30 × 50 mm. At the end of four hours the pollen reactions were questionable or

not marked whereas the emulsions were almost as marked, very itchy, and were still visible up to thirty-six hours, in one of the recipients.

All controls, that is, of the four antigens used, were negative except for a small hemorrhage caused in two instances.

A later attempt using different bacterial emulsions only as well as the autogenous strains failed to give the wheal formation but did give definite areolas with the two strains of the patient's staphylococci only.

Such difficulty had been experienced in attempting to increase the dose of extremely dilute emulsions that an attempt was made to determine whether this strain of staphylococcus produced a soluble toxin comparable to the toxin of the streptococcus of scarlet fever. Dr. Freida Fraser of the Connaught Laboratories, University of Toronto, kindly undertook this and from animal tests reported that there was such a toxin, and to this toxin I have been able to obtain a 30 × 30 mm. reaction in twenty-four hours by intradermal tests on the patient.

Dr. Fraser has attempted to detoxicate this with formalin in the same manner as introduced by Ramon in his anatoxin for diphtheria prevention. At the present time I am attempting slow immunization with the detoxicated solution.

The case has presented a number of unusual characteristics which I have not previously encountered. The loss of her thyroid gland and the loss of the uterus and adnexa possibly are factors. Her reactions are peculiar; when severe she is not under undue respiratory distress but complains that her lungs, or usually a part of her lungs, feel like cotton wool. That phrase was, as far as I know, invented by herself and not obtained from medical sources. At the same time I have more than once seen her bring up blood-streaked sputum in fairly free amounts. The general distress, flushing with perspiration and tremor, has often been marked. What rôle the free toxin plays seems doubtful.

In reporting local passive transfer to a recovered culture I felt that some indication as well ought to be given of the unusual features of her allergic manifestations. This I have tried briefly to do.

(For discussion, see page 394.)

INCIDENCE OF DIABETES MELLITUS IN ASTHMATIC PATIENTS*

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IT OCCURRED to us that with the type of patient coming to an asthma clinic we were seeing individuals with the syndrome of diabetes mellitus very rarely, actually six definitely diabetic patients of 4,000 allergic patients treated both in clinic and private practice, over a period of ten years.

It is the routine of the clinic that all patients have a history, physical examination, intradermal tests, nose and throat examination and x-ray studies of teeth, sinuses and chest.

In this group of 4,000 patients we have found but six who have both diabetes mellitus and an allergic condition. Of these, three were asthmatic; one was late hay fever with seasonal asthma; one, early and late hay fever, and one questionably asthmatic and in addition had hypertension. The case histories are briefly abstracted as follows:

CASE 1.—S. F. Aged 57 years, white, male. First seen on September 25, 1923, and came for asthma of twenty years' duration. Has been worse the past year. Asthma continuous with more severe attacks every few hours. The lungs were full of squeaking râles; blood pressure 150/94. The urine contained 1.25 per cent sugar. There were no real positive skin reactions. Has been seen intermittently during the past eight years, having attacks of asthma. During a period of three and one-half years between 1925 and 1929 was practically asthma-free. Nasal examination showed bilateral polypi. The x-ray showed a cloudiness of all sinuses, markedly so, the left antrum. Lungs showed marked root shadows with the peribronchial thickening of asthma. During the time of observation at the clinic he had been on the Jefferson wards for treatment of diabetes mellitus. During observation at the asthma clinic the urine had been sugar-free on nine occasions. In 1929 he had a papilloma of the bladder removed by fulgeration.

CASE 2.—L. Z. Aged 32 years, white, female. Seen October, 1924. Referred from the ward service where she had been treated for diabetes for three months. Was discharged on an insulin dosage of 20 units three times daily. She had had asthma for eighteen years, never severe, and mild attacks occurred about once a month. There were no positive skin reactions. Asthmatic râles were never heard. She was

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observed for one and one-half months during which time she complained of mild asthma. She had a slight reaction on intradermal test with insulin.

CASE 3.—C. T. Aged 47 years, white, male. Patient was decidedly overweight, and had a history of rheumatic gout yearly for eight years, with onset in joint of big toe. Was first seen in June, 1929. Blood pressure 130/90. There were no râles in the lungs. The intradermal tests at this time were a marked plus reaction to 0.001 grass, marked to 0.01 plantain, moderate to marked to 0.001 ragweed, and a positive eye reaction to 0.01 grass. In 1930 the intradermal reactions were marked to 0.001 grass, slight to 0.01 plantain and marked to a 0.001 ragweed. The eye reaction was slightly positive to a 0.001 grass. Three blood sugars done in September and October varied from a maximum of 234 mg. per 100 c.c. in the middle of September to 145 mg. per 100 c.c. on October 3. In 1931 skin reactions were as follows: slight to 0.001 grass, moderate plus to 0.01 grass, negative to 0.01 plantain, and moderate to marked to a 0.001 ragweed. The eye reaction to a 0.001 grass was negative and to a 0.1 grass positive. The blood sugar varied from 242 mg. on February 26 to 172 mg. on April 13, 1931.

CASE 4.—C. G. Aged 51 years, white, married, female. First seen May 22, 1930. Applied for prophylactic treatment for late hay fever with asthma. She at this time had marked reaction to 0.001 ragweed, and during the course of treatment she had two immediate constitutional reactions to small doses and believes she was much improved with treatment though she spent two weeks in bed because of asthma. In 1931 she showed a marked reaction to 0.001 ragweed and a positive eye reaction to the same strength. At the time of these tests the blood-sugar reading two hours after lunch was 227 mg. per 100 c.c. of blood.

CASE 5.—F. B. J. Aged 56 years, white, male and a blaster by occupation. First seen February 16, 1931. Chief complaint at this time was glycosuria. Gave a history of having had rheumatic pains twenty-nine years before and for the past three months shortness of breath and coughing at bedtime and in the morning, on arising. There were sonorous râles throughout the left chest, piping râles and wheezing throughout the right chest. The sinuses were very clearly transilluminated. Teeth showed slight pyorrhea, the urine 2.5 per cent sugar and a light cloud of albumin. Blood pressure 146/90, weight 179 lb. The fasting blood sugar on February 18 was 174 mg. per 100 c.c. of blood. Wassermann test was negative. Skin tests were not done at this time.

CASE 6.—Mrs. M. C. Aged 59 years, white, female. First seen December, 1924, with a history of having had asthma for two years. She complained of shortness of breath on exertion and at night. Had never

had any severe attacks. Did not give any positive skin reactions, although complete testing was not done. Blood pressure 164/80, weight 166 lb. February, 1925, two months later patient was visibly dyspneic. There were no râles in the lungs. Blood pressure 140/78. Seen again May 4, 1925, complaining of much dyspnea on exertion. The lungs were still clear. At this time there was found a phlebitis of varicosed vein of the left thigh. On October 3, 1925, blood pressure was 136/80. On May 1, 1926, blood pressure was 115/72. There were no râles in the lungs. On May 7, 1927, she still complained of asthma and again on December 3, 1930. For the past month has been complaining of thirst, weakness, passing of urine at night, passing of large quantities of urine, also had pruritis vulvae. Patient was markedly dyspneic, but there were no râles in the chest. Blood pressure 150/80, urine contained 5 per cent sugar and had a light cloud of albumin. Blood sugar was 200 mg. on December 16. The urine contained 1.6 per cent sugar at this time. Blood pressure was 160/90. On January

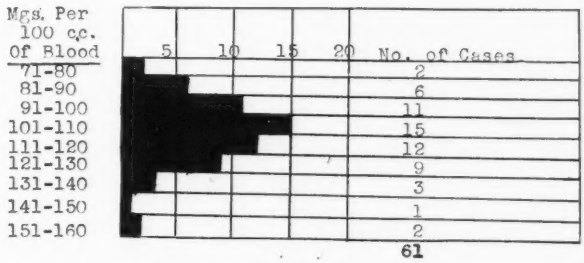

Fig. 1.—Blood-sugar readings.

5, 1931, blood pressure was 134/60, weight 132 lb., and urine was sugar-free. On January 26 urine was still sugar-free. On daily home tests it was also sugar-free and patient was feeling fine. February 19, weight 138.5 lb.; blood pressure 180/90. Patient having epigastric distress and showing sugar in the urine. On April 14 weight was 140.5 lb., blood pressure 140/70, faint trace of sugar in urine and patient was feeling fairly good.

To convince ourselves further that asthma and diabetes mellitus rarely occur together we thought it advisable to do blood-sugar determinations on a group of allergic patients under circumstances which were not ideal for diabetic patients, that is, all patients were over thirty years of age, and most over forty years, overweight and non-fasting.

Of this group, blood-sugar readings ranged as shown in Fig. 1.

DISCUSSION

Case 1. Findings in the chest were definitely those of asthma, but there were no real positive skin reactions. The upper respiratory

tract findings were those seen in asthmatics, as were also the x-ray findings of the chest.

Case 2. Patient in whom there were no chest signs of asthma, and intradermal tests were all negative, except for a slight reaction to insulin.

Case 3. Patient in whom with the development of diabetes, skin reactions apparently decreased and then with treatment and lowering of the blood sugar, the skin reactions further decreased in severity. This patient had never had asthma, but the seasonal history and intradermal reactions are indicative of an allergic state.

Case 4. The patient definitely allergic by history and intradermal reactions.

Case 5. Patient whose chief complaint was that of glycosuria. Had had no marked symptoms whatever, and the chest signs of asthma were found during routine examination, though the history of dyspnea and cough seem to corroborate the physical findings. Of course the history of short duration and the findings may be those of chronic bronchitis. Skin tests were not done.

Case 6. This patient is questionably asthmatic. We could not corroborate definitely her diagnosis of asthma by chest signs, and she did not have any definitely positive skin tests. Her dyspnea and chest distress improved when the urine became sugar-free and reappeared with the reappearance of sugar in the urine.

CONCLUSIONS

1 This preliminary study in asthmatic patients whose sugar determinations were done in nonfasting states, in middle-aged, overweight and allergic patients, indicates their ability readily to utilize carbohydrates, as pointed out by W. R. Ohler in a personal communication to Joslin.[1]

2. Our findings are similar to those of Rackemann and Walker, both quoted by Joslin, who report six cases of asthma in diabetic patients, in that diabetes mellitus and asthma do not commonly occur in the same individuals.

3. In view of the fact that both diseases occur in the same individual at the same time and both the diseases are typical in their manifestations, it is difficult to understand why skin reactions should apparently decrease with the onset of diabetic symptoms and why the asthma should improve with treatment of the diabetes.

REFERENCE

1. Joslin: Treatment of Diabetes Mellitus, 1928, ed. 4, p. 733, Lea and Febiger, Philadelphia.

(For discussion, see page 400.)

A MULTIPLE SCARIFIER FOR ALLERGIC TESTS*

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THE numerous instruments used for scarification have all the common objection of producing an abrasion which lacks uniform length and depth. To compare the size of the wheal produced in sensitive individuals by related materials, as giant and short ragweeds, an instrument was designed with which six incisions of practically uniform length and depth can be made simultaneously.

The instrument is a rectangular metal box, 9 cm. long, 2 cm. wide, and 2½ cm. high, open at one of its long sides. At either end are finger holds where the thumb and third finger may hold it securely

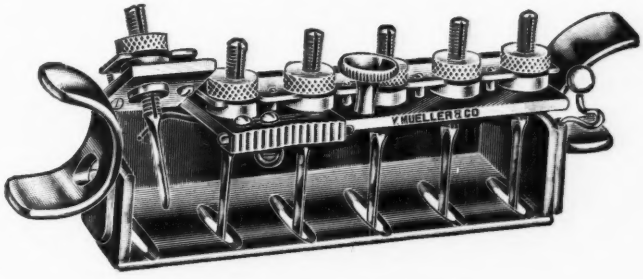

Fig. 1.—Multiple scarifier × ⅔.

in place and exert pressure over the underlying skin. The base is flanged in front in an upward curve to prevent the pressure of a sharp margin on the skin. It has six elliptical perforations 15 mm. apart just beyond the flanged portion through which the knives pass when they are pressed down.

The back of the instrument has two wire springs at either end supporting the top which bears the knives and preventing them from coming in contact with the skin unless pressed down. The top is hinged to the back. It is divided transversely into a long portion bearing five knives and a shorter part with one knife. These two parts are connected by a sliding clamp so that either one, five or six incisions may be made simultaneously. The top has near its free edge six perforations at 15 mm. centers. A projecting guidepost in each of these fits into a longitudinal channel cut in the threaded shaft of each knife to prevent its rotation from the cutting axis. In addition to these guideposts, the knives are held in place by six knurled

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set screws fixed to the top of the instrument and threaded to their shafts. The blades are 3 mm. in width, sharpened on both edges and terminating in a razor-sharp rounded cutting end. Their length is adjusted by rotating the knurled set screws previously mentioned. We use a length of blade about ½ mm. beyond the plane of the base. One of the end knives is adjusted to this cutting length. The cover is then raised until the point of this blade is just visible as one sights along the base. The other blades can then be adjusted by rotating their set screws until their blade points also are just seen. With ordinary care this adjustment need be made only once every two months when the blades require to be removed for sharpening if they are subjected to frequent daily use. When not in use a simple lock at one end keeps the top slightly elevated, preventing dulling of the blades.

The incisions made are 1½ mm. in length with sharp, clean-cut margins. The optimum depth obtained with firm pressure and with the blades adjusted has already been described. We have found that a fine bleeding point is visible in the center when the margins of the cut are separated, but there is no active bleeding. In cases of marked dermographism when slight skin trauma produces a wheal, there has been distinctly less wheal formation with this type of sharp cut than that obtained with other instruments generally used. In addition, because of the arc described by the knives and possibly because of the firm pressure of the base, very little pain is felt. This has been a distinct advantage in dealing with children and with nervous adults who are not only apprehensive of pain but of the sight of a sharp surgical instrument. It has been successfully used for a year at the Allergy Clinic of the University of Illinois College of Medicine and by several of its members in their private practice.

SUMMARY

A description is given of a scarifier producing six incisions simultaneously of practically uniform length and depth and with a minimum degree of pain and skin trauma.

Society Proceedings

THE SOCIETY FOR THE STUDY OF ASTHMA AND ALLIED CONDITIONS

SEVENTH ANNUAL MEETING, ATLANTIC CITY, N. J., MAY 2, 1931

PRESIDENTIAL ADDRESS

THE FUTURE POLICY OF THIS SOCIETY

J. A. CLARKE, JR.
PHILADELPHIA, PA.

THIS society was formed eight years ago to promote the study of asthma and allied conditions. During this time there has been a decided increase in the interest of the general profession in the subject. Both this society and our sister organization have grown numerically, beyond the hopes of their founders.

Many books on the subject of asthma and allied conditions are now available, and more are in the course of preparation. Our own magazine is well established.

Unfortunately there has been no corresponding increase in our knowledge of the subject. The older clinics are using the same methods as they did in 1923. The usual false hopes have come and gone, now, as they have for many years. One is forced to the conclusion that our present knowledge of the subject has reached its full development, and that further progress must wait upon the discovery of some radically new and important idea. This means that the treatment of asthma in the hands of most members of this society is essentially the same and that it should be comparatively easy to formulate some standard plan of treatment which would meet with the approval of the society as a whole.

This standard plan should be as simple and fundamental as possible, but should contain the minimum amount of work to be done on each asthmatic.

Such a plan, consistently followed, by men of average ability, should result in decided improvement in at least 60 per cent of all those suffering from asthma, and about one half of this number should be changed from invalidism to full capacity for useful employment. So far this knowledge is available to only a small fraction of the population. Even in the large medical centers there are still many asthmatics who have never been tested, and there are large cities where

no one is properly equipped to give the sufferers the full benefit of those advances which have been made during the past fifteen years. Much progress in the dissemination of this knowledge has already been made.

Furthermore, asthma will probably become more frequent. It is decidedly hereditary and since it has never been easier for a person who is partially incapacitated to rear a family, many asthmatics are becoming heads of families who, fifty years previously, would either have succumbed or failed to have married. Also since allergic manifestations are common in the early years of life, it is undoubtedly true that many children who would formerly have perished in infancy are, thanks to child health agencies, surviving, outgrowing their asthma and later reproducing themselves. Certainly the discomfort and suffering from asthma are enough to interest the humane agencies. In the present state of unemployment, the economic loss of days' work, lost because of illness, is not as important but none of us expects this state of affairs to last long.

The question can now be raised, Shall this society limit its functions to the selection of members and the holding of two meetings a year? Our influence in this direction has already been felt, and the executive committee feels that a number of young men have been stimulated to do better work in order to become eligible to membership in the organization. The interchange of ideas in the social contacts of these meetings has a worth that cannot be calculated.

Should the society do more? Should we make an effort to hasten the time when any asthmatic can receive as good treatment as the sufferer with tuberculosis, for example?

If the answer is "yes," how should we proceed? Before we can place the matter before any health agency, private or public, certain problems must be solved.

The first of these is the standard form of treatment already mentioned.

The second is proper materials to do the work. At the present time there are as many different solutions and powders available as there are manufactures. These are not interchangeable. It would seem that with all the experience that we have had, that the society could, by means of a committee, decide upon some definite mode of manufacture which would result in potent, uniform materials whose stability could be accurately forecast. Any manufacturer using such methods should have the preparations tested, and if satisfactory, should receive public approval by the society. The U. S. Bureau of Standards, the publishers of *New and Nonofficial Remedies,* and the Society for the Study of Allergy would undoubtedly be glad to cooperate. Until uniform solutions and methods can be established, the present chaotic state of individual effort will continue.

The next need is the education of physicians in the special work. There is probably no branch of medicine in which the fundamental principles of the treatment are simpler than they are in allergy. In fact this simplicity has been a curse because it has given men false confidence in their own and in other's ability. At the present time there are a few courses given in the larger graduate schools. Such courses are didactic and theoretical and, in my opinion, wholly inadequate unless followed by some practical work in a busy asthma clinic. No better means of education could be found than the asthma clinics conducted by the various members of this society. Two or three months' attendance at one of these clinics should adequately prepare a man to go out and establish an independent clinic. Our society could prepare a list of such clinics with the number of openings in each clinic and so act as a clearing house between the men desiring such instruction and the clinics.

An effort should be made to list all clinics which are doing good work. Modesty is not a lost virtue and I have no doubt that there are good men who have educated themselves and who are doing good work with their candle under the traditional bushel. The leaders of these clinics should be urged to join our society and make their clinics available for the instruction of others.

When we have standard solutions and facilities for educating workers, we shall then be in a position to go to various boards of health and heads of hospitals and point out to them their deficiencies and how they may remedy them. The opportunity for this society to be of real service to the country is undoubtedly present. I know of two centers of population in both of which there are Class A medical schools and in which there is no place where the modern treatment of asthma can be obtained. At the present time two recent graduates are endeavoring to fill the gap. After two years, if they do not become discouraged before, they may have as much knowledge and experience as they would have had, had they spent two months at an established clinic.

Most of us will agree that the work in asthma will have to be carried out by specially trained men. The general practitioner cannot devote the necessary time for the fees which he receives, nor does he see enough cases to obtain the experience which is so helpful. The long-suffering public has the idea, not without some justification, that it has enough specialists to support. The amount of time which each asthmatic requires from his specialist is great compared to the time which other specialists are called upon to give. Furthermore the results cannot be accurately forecast as in the surgical specialties. It would seem that the society, in bringing this knowledge to the attention of the public, should also suggest a practical method of retailing these benefits. The majority of sufferers are neither poor nor

wealthy, and a means should be devised to treat that great class of persons who are quite capable of paying for ordinary office visits, but who are not able to pay to the allergy specialists those fees which he must charge. It is suggested that pay clinics be established to give the expensive tests and treatments and that each of these clinics be prepared, wherever possible, to pass the routine treatment back to the referring physician. It will be necessary to pay the doctors working in these clinics. There are not enough wealthy asthmatics to support the corps of physicians necessary to give treatment to their less fortunate brothers. On the other hand, the asthmatic is not nearly so hard hit financially as the tuberculous patient and the majority can and are anxious to make a substantial contribution. While it will probably be necessary to have these clinics sponsored by philanthropic or public agencies, they should eventually become self-supporting, but rarely, if ever, profitable.

The next step is the education of the general practitioner. He should be taught that his unskilled efforts to utilize the expensive materials sold him by detail men are not likely to be of benefit to his patient or of profit to himself. He should be told the limitations of our treatment as well as its possibilities, and he should be encouraged to work in cooperation with the specialist or the special clinic.

The most important of all, probably, is the education of the public itself. There is a feeling today that the skin tests are much like a Wassermann or a urine analysis and can be performed by anyone with a small outlay for equipment. So when the family physician with a few old food powders scratches their skin, they are under the impression that they have had the advantages of the latest that science has to offer. The need of special training in the technic and the interpretation of the skin tests and the cost of maintaining a properly equipped office should be stressed. When the public demands special attention for asthma and then finds that facilities are available for anyone regardless of his financial standing, we shall not only make a distinct advance in our own special field, but shall also help to solve the perplexing question of the dissemination of practical scientific, but expensive treatment for other fields.

There are a number of precedents for a professional and public campaign of education. The oldest and most successful of these is that against tuberculosis. Operating as a part of the Red Cross, it enlisted the services of the most influential men in every community. The venereal campaign was conducted wholly by governmental agencies. The heart association consists of the leaders of the profession and other selected, influential laity. Orthopedic conditions in children are under the care of business and fraternal organizations.

If the society decides that the propagation of the faith is one of its legitimate functions, it would seem fitting and proper that three

committees be selected at this time: the first committee to standardize the manufacture of diagnostic and therapeutic materials, to determine the minimum physical requirements of an asthma or allergy clinic and to suggest a uniform method of treatment; a second committee to devise ways and means to educate the future allergy specialists; a third committee to collect data on the incidence of asthma and to suggest a practical scheme which will result in the establishment of asthma clinics in every large center throughout the country.

We should hope for preliminary reports from these committees at the December meeting with final action a year from now. We can do nothing at the present time other than to appoint the committees.

DISCUSSION

DR. JOHN MURPHY, PHILADELPHIA.—I want to compliment you on sounding an interesting note in this meeting. I think we have all been interested in the fact that there is no standard form of manufacture for the different extracts used in our work. The Hygienic Laboratory in Washington is not interested in the potency of pollen extracts so much as in their purity. In other words, they would like to know that a ragweed extract is a ragweed extract; they do not care whether it is a 100 per cent solution or not. Your line of approach here today is certainly a step in the right direction, and I should like to add my personal thought that some action be taken along this line.

DR. AARON BROWN, NEW YORK CITY.—Last year the New York Academy of Medicine was interested in solving the problem of the chronic asthmatic. For this purpose we had hopes of interesting somebody with enough money to support two hospitals, one for children and one for adults, with a capacity of seventy-five patients for each unit, patients to be kept under observation for three months or longer. At the same time, we drew up plans for the minimum requirements for a standard asthma clinic and arranged for a clearing house for exchange of information. Through the clearing house, we save duplication of work. We know that patients go from one clinic to another. We also devised a minimum uniform history chart for the use of approved clinics. An approved clinic is one using:

1. Uniform history chart,
2. Facilities for complete testing,
3. Facilities for nose and throat work,
4. Facilities for x-ray study,
5. Social service work.

The Secretary of the Academy informed me they had not yet found anyone with sufficient money or interest to finance the hospital idea, though the Academy approved it. While we have a skeleton organization of the various chiefs of clinics which could be put into effect at any time, and while these chiefs of the various clinics have accepted the minimum standard requirements for the approved clinics, as well as the idea of the exchange of information (we believe that information obtained from case studies for three months should be available to any clinic that applies for it), we have gone no further at present.

I was also interested, recently, in organizing a research laboratory for the preparation of test materials on a nonprofit basis, and for the organization of an institute not only for the study of the atopins but also for clinical research, but unfortunately that scheme fell through.

I believe the only way in which we can make progress in this subject is to permit everyone interested in the subject to have the use of the best available ma-

terials. At the present time, we do not use a common method; one uses the scratch method, another the intradermal, one prepares his own materials, another uses commercial, and the result is that we get together, we talk about a lot of things, but we do not advance the subject sufficiently. If everyone used standard materials, we could advance the subject ten times more rapidly than we are doing today.

PRESIDENT CLARKE.—There is no doubt at all that the interest in allergy is progressing very fast over the country. There is also no doubt that the solutions which are put out by commercial houses are becoming much more valuable, much more reliable. The whole question is whether this Society should make an effort to hurry up the time when the knowledge will be generally disseminated and whether such an action by this Society would not save a lot of individuals and a lot of communities the expense and the trials and the trouble of making false starts with poorly equipped and poorly trained asthma clinics.

When I first went to Philadelphia ten years ago, I found there had been a number of abortive efforts to establish clinics and that there was considerable feeling at that time against the whole method of investigation. We have had to live down, so to speak, a bad reputation due entirely to overenthusiasm and lack of training of the men who went into it. If there is no further discussion, we shall take it as an indication that the Society believes the country is receiving the maximum benefits from the present method.

DR. W. T. VAUGHAN, RICHMOND.—If I may enter the discussion at this late moment, I think the need for such a program is really more acute than most of us realize. The laity is becoming allergy-conscious. We are all of us surprised at the number of people who know what allergy is. Personally, I believe we have reached the stage where unless some definitely systematized program is undertaken, there will be a lot of semicommercial exploitation with so-called allergy clinics. It is much easier to lead the movement into the right channel now than to break up such organizations later. Any work this Society would do should have the moral support of our sister organization.

The Effect of Bronchial Asthma on the Heart.* LEO H. CRIEP, M.D., PITTSBURGH, PA. (Abstract.)

A. Effect of long standing bronchial asthma on the heart. Reports in the literature bearing on this subject are not in agreement. Kahn and Unger conclude that there is some cardiac involvement, while Alexander can find no evidence of cardiac damage resulting from long standing bronchial asthma. A complete cardiac study of fifty cases of proved bronchial asthma is presented including clinical examination, vital capacity, venous pressure, roentgen ray, and electrocardiographic investigation. The results of this study indicate that bronchial asthma does not have a damaging effect on the heart.

B. Effect of the acute paroxysm on the heart. The symptoms of asthma are in a way those of mild asphyxia. Asphyxia and anaphylaxis in the guinea pig are associated with a definite train of cardiac changes. It is logical to assume such changes may occur in a lesser

*From the Department of Internal Medicine and the Clinic of Applied Immunology, University of Pittsburgh, Pittsburgh, Pa.

degree in bronchial asthma. Twenty patients were observed. Twelve were examined clinically and of these, one showed premature beats during the attack. Eight were electrocardiographed. Of these, one showed delay in auriculoventricular conduction, and the second, frequent premature beats. It is concluded that if the attack is sufficiently severe, functional cardiac changes may occur.

DISCUSSION

DR. KERN, PHILADELPHIA.—As further evidence of functional derangements, and going a step further than the cases shown by Dr. Criep, I would like to refer to a patient, thirty-five years of age, who had severe asthma from the age of twelve, and in whom there developed attacks of angina pectoris with electrocardiograph abnormalities in the form of T-wave changes. Relief of asthma by avoidance of the substances to which he was sensitive, resulted in complete relief from his angina pectoris and the return of the electrocardiographic tracings to normal.

Staphyloccccus Filtrates, Toxic and Nontoxic; Their Use in Intradermal Studies. EARL BURKY, M.D., BALTIMORE, MD. (Abstract.)

Filtrates of staphylococcus cultures recovered from various eye conditions have been studied by means of intravenous and intradermal injections in rabbits and intradermal injections in human beings.

Filtrate Ha recovered from a case of chronic conjunctivitis kills rabbits within twenty-four hours after injection of 0.2 c.c. per kilo of body weight. Injected intradermally into rabbits it produces erythema and swelling, followed by necrosis. One or two intradermal injections produce immunity. Immunity is shown by the ability to withstand multiple lethal intravenous doses of toxin, development of precipitins for the filtrate in the immune serum, and absence of necrosis following intradermal injection.

Strain Fs recovered from a case of recurrent styes produces no lethal toxin for rabbits. In this respect it is similar to strains of staphylococci recovered from normal eyes. When injected intradermally in rabbits, these filtrates produce erythema and swelling without necrosis. Repeated injections produce an Arthus-like prenomenon. Following the development of the Arthus-like phenomenon the animal is immune to lethal doses of Ha toxin. No precipitins appear in the serum of these animals.

These filtrates diluted 1-10, when injected intradermally into human beings produce erythema and swelling. In human beings arbitrarily classified as normal, strain Ha produces reactions averaging 4 to 6 cm. Strains Fs and DI produce reactions averaging 2 to 4 cm. In individuals classified as abnormal, with a history of focal infection, chronic colds, conjunctivitis, and skin infections of the acne type, the reactions produced by all strains are about twice as great.

DISCUSSION

DR. LOUIS TUFT, PHILADELPHIA.—I should like to call attention to some work done with staphylococcus filtrates at the Research Institute in Philadelphia, where Drs. Greenbaum and Harkins have been using staphylococcus filtrates for intradermal tests. They have found that these cases give positive skin tests in a large proportion of cases, and further, that intradermal injection in these individuals seems to produce a much better type of immunity than injection by subcutaneous or intramuscular routes. That corroborates some previous work I have done on comparison of the intradermal test with the other methods.

DR. A. F. COCA, NEW YORK CITY.—I have known about this paper through personal communication with Dr. Burky. It seems to me, if I have not made a mistake, there was some question in Dr. Burky's mind as to whether the filtrate contains a true toxin or not. In other words, some of the reactions that he obtains both in the animal and in the human may be like the Schick reaction, that is, the effect of a toxin; and there may be other reactions that are those of hypersensitiveness. In this case, the situation would be the same as with the filtrates of *Streptococcus hemolyticus*. Some of these filtrates have very little bacterial protein, so that the reactions of hypersensitiveness are uncommon. They are uncommon anyway, in young children, but as the children grow older and immunity to the toxin sets in, there are fewer of the reactions to the toxin and more of the allergic reactions to the bacterial proteins.

If I remember rightly, Dr. Burky carried out skin tests on human beings and noticed this same relationship; that is, the reactions to the filtrates increased with age. However, these may have covered up an immunity to a possible toxin in the fluid. These two elements can be separated chemically; according to Ando, the protein constituents of the scarlet or Dick toxin can be precipitated by acid, leaving the true toxin almost pure and with that treated filtrate, fewer reactions are obtained in the older children and correspondingly more in the younger ones. Similar treatment of the filtrate which Dr. Burky is studying might help decide whether a true toxin is present in it.

DR. GRAFTON TYLER BROWN, WASHINGTON, D. C.—For some time now, I have been testing all of my asthmatic bronchitis patients intradermally with autogenous vaccines and bacterial filtrates prepared from each of the organisms isolated from cultures of the nasal secretion, throat, and sputum. *Staphylococcus aureus*, *Streptococcus hemolyticus*, and *Streptococcus viridans* are the organisms most commonly encountered in these cases. The staphylococcus vaccines give positive reactions much more frequently than the streptococcus vaccines, whereas with the filtrates it is just the reverse, namely, the streptococcus filtrates react more frequently than the staphylococcus filtrates. The vaccines and filtrates which give positive reactions are selected for treatment, and those which fail to react are discarded.

DR. BURKY.—Because of the time limitation I did not discuss the skin testing in human beings, but I can agree with all that has been said about the intradermal test. There is definitely a considerable reaction to the Ha strain filtrate. In human beings arbitrarily classified as normal this reaction is about 4 to 6 cm.

In people whom we have arbitrarily classified as abnormal there is a tremendous intradermal reaction which may involve the whole forearm, and in addition such individuals react with an immediate wheal and erythema with both toxic and nontoxic filtrates. Such people when given two to three intradermal injections lose the immediate type of reaction. The delayed reaction continues, but with much less intensity. I believe the reason for the delayed reaction is that the filtrate

is a toxin similar to diphtheria toxin. In addition there is an element of hypersensitivity to this toxin because the reaction continues and does not decrease as does the reaction to diphtheria toxin.

Some Observations on Infective Asthma. ROBERT A. COOKE, M.D., NEW YORK CITY. (Abstract.)

Cases of infective asthma are compared with asthma due to substances (foods or air-borne substances) which give positive cutaneous test reactions. In the infective group up to the age of ten years 82 per cent have a positive antecedent history of allergy, while in the so-called sensitive group of the same age the antecedent history is positive in 67 per cent. For the entire group the antecedent history is positive in 45 per cent of the 106 infective cases and in 52 per cent of the 183 sensitive cases.

In a study of the eosinophil distribution in 131 active cases, the blood eosinophilia is somewhat more frequent and certainly higher in the infective than in the sensitive cases. The presence of abundant eosinophil cells in the nasal or bronchial discharge even in cases with normal blood indicates an histogenous origin of these cells. Tissue eosinophilia is regarded as an indication of an allergic response. Hence in the purely infective cases it represents an allergy to bacterial substances.

The studies of heredity and of blood indicate that infective asthma must be regarded as a form of allergy, though not identical with that seen in the cases with positive skin reactions.

DISCUSSION

DR. ROBERT CHOBOT, NEW YORK CITY.—In going over a series of 100 cases, mostly children, we found in many cases that as a child grew older and the incidence of infection grew more as a factor in the causation of his asthma, the blood eosinophils paralleled just what Dr. Cooke reported here today.

Of course, our series of cases was not nearly so well worked up as that of Dr. Cooke. However, it is interesting to see that the young child without infection has usually an eosinophil picture which is low, but as an infectious element enters into the clinical picture, the eosinophil count gradually rises.

DR. T. D. CUNNINGHAM, DENVER.—I want to raise the question whether eosinophilia is due to irritation of the mucous membrane. In talking to skin specialists about this type of case, they say this increase of the eosinophils is very common in almost any form of skin irritation.

DR. JOSEPH HARKAVY, NEW YORK CITY.—Several years back I had the impression, which Dr. Cooke confirmed today, that the presence of eosinophilia in the blood was not exacting enough to differentiate between atopic asthma and infectious asthma.

Two years ago, I presented before this Society a group of fatal cases of infectious asthma. I stated that in those cases microscopic sections showed such a tremendous outpouring of eosinophils within the bronchial wall, in the degenerated, necrotic mucosa of the bronchi, as well as in the mucous cells of the

bronchus, that I felt that eosinophilia as such was no criterion of the presence of atopy and indicated some form of allergy to infection.

Along the same lines, I was struck recently by a very interesting finding in a case of heart disease. This person whom I had observed for a number of years began running a temperature which I could not explain definitely other than that she had a mild attack of rheumatic fever. She had an old mitral stenosis. As she got better and her temperature dropped, I brought her to a consultant cardiologist.

I had a blood count made, and her blood showed an eosinophilia of 16 per cent. I was astonished and discussed it with Dr. Rosenthal. He told me that in doing blood counts on convalescent cases of rheumatic fever, he repeatedly noted such counts, some of them going even higher.

This finding interested me a great deal because of the allergic point of view which is being stressed at the present time in respect to the nature of rheumatic fever. Dr. Cooke's findings, my own, and those of others, seem to be a keynote to the relation of allergy to infection, and as we come to know more about it, we shall begin to realize that the mechanism is the same. As yet it is not very clear whether it is an individual member of the bacterial proteins or a combination of bacterial proteins that brings about the reaction.

DR. GRAFTON TYLER BROWN, WASHINGTON, D. C.—Somewhat in line with Dr. Cooke's findings, a study of 167 patients showed just as high an average of eosinophils in the blood in the nonatopic or bacterial cases as it did in the true atopic ones. Also, most interestingly, the highest percentages we saw, from 20 per cent up, were all, I believe, in the bacterial cases.

DR. ROYCE PADDOCK, NEWARK, N. J.—I used to think that the presence of eosinophils in blood and sputum was a sign of hypersensitiveness to an outside factor and that their presence more or less excluded infection, but in the last year or two, I have come to think the other way, that is, that eosinophils in the sputum are just as often present in purely infectious cases as in the atopic or uninfected type.

I think this is very important because if we take the cases of so-called vasomotor rhinitis, the idea is widespread that they are due to outside factors. The same assumption is apparently made from the pathology demonstrated in the articles (such as Hansel's) quoted by Dr. Cooke, that they are not caused by infection because there is no large amount of polymorphonuclear cells found in the tissue. If it is true that eosinophils may represent the cellular reaction to an infection, they are just as much a sign of hypersensitiveness to infection as they are to outside factors such as dust. It opens up an entirely different attitude toward these cases.

There is one point about these cases where skin tests are negative and the eosinophil count in the blood or sputum is high; there seems to be a possibility that some of these cases are cases in which the extrinsic factor has not been found. The symptoms may be due to some factor we have not in bottles yet and so cannot test the skin with it. This seems to be sort of a loophole which has not yet been excluded. It stands a little in the way of our being sure that some of these cases are due primarily to infection.

DR. COOKE.—It is indeed true that a blood eosinophilia is a not uncommon postinfective reaction. An eosinophilia in the blood, therefore, does not necessarily mean asthma but it does seem to indicate a peculiar immunological response and may be regarded as a manifestation of bacterial allergy. A tissue eosinophilia may also be regarded as a localized allergic response. It is significant that it does not occur frequently in the chronic suppurative sinus infections without asthma. In but one of the small group of nine such cases in the series presented was there evidence of any unusual eosinophilic response in the infected tissue.

The Effect of Tonsillectomy in Allergic Conditions. STEARNS S. BULLEN, M.D., ROCHESTER, N. Y. (For original article, see page 310.)

DISCUSSION

DR. RACKEMANN, BOSTON.—I found the same thing some time ago as did Dr. Bullen, which rather indicated to me that it is better to leave the tonsils in than to take them out.

At the same time, there is no doubt tonsillectomy is of value in a small number of cases, particularly with children with big tonsils, who have asthma in isolated attacks. In a few of such cases, the removal of the tonsils will stop the attacks and do the child a lot of good.

DR. CAULFEILD, TORONTO.—I think it was Dean of St. Louis who at one time stated that weekly colds in children were caused by hypertrophied adenoids and infected adenoid tissue. We must bear in mind that adenoids is a common form of focal infection. Later Dean changed his mind and said that before the adenoids or tonsils are touched, allergy must be ruled out. I think that is the attitude we all should assume. While we should not give too much attention to the removal of tonsils and adenoids, a happy medium can be struck. There are children who have eliminated the exciting elements, arranged their diets accordingly, and the only thing that seems to be left to cause a paroxysm is infected adenoid tissue. I do think that infected adenoid tissue is a cause of paroxysm, particularly at night when the mucosal secretions collect in the naso-pharynx. The need of adenoidectomy is indicated in such cases.

DR. W. T. VAUGHAN, RICHMOND, VA.—When the tonsils are out, we pay little attention to the history of onset as related to nose and throat operations. Occasionally the patient dates the onset of his allergic condition to a tonsillectomy. It would be well if we could compare the frequency of this phenomenon with the frequency of no allergic flareups following such operations. In my experience, it is not frequent and may be coincidental, but the patient who does experience his first symptoms shortly after the operation is very certain that the operation was responsible.

Dr. Huber last year reported on an investigation in which he found that around 10 per cent of his asthmatic and hay fever patients dated the onset of allergic manifestations from a nasal operation or tonsillectomy. It is interesting to wonder what happens from an allergic point of view.

DR. LESLIE N. GAY, BALTIMORE.—For several years I have felt that the onset of hay fever or pollen asthma has been the aftermath of a nasal operation performed during the time when pollen saturated the atmosphere. In the patients whom I have in mind a history was obtained pointing to a hereditary factor, the father or mother having had either hay fever or asthma. For this reason I believe one should obtain a careful history as to whether or not such hereditary factors exist before an individual is subjected to a nasal operation in the midst of the pollen season. Of course, this precaution is not so necessary when the atmosphere is free from pollen.

I am unable to explain this mechanism of sensitization.

DR. JOHN MURPHY, PHILADELPHIA.—Dr. Gay's comments bring up the point concerning an optimum time for operative interference in the so-called allergic individual.

DR. W. T. VAUGHAN, RICHMOND, VA.—Just one interesting case I saw recently: A woman in her forties, who had had a tonsillectomy for a vasomotor rhinitis, immediately after the tonsillectomy developed her first asthma which she has had ever since, and, curiously, she was not sensitive to anything. She was what we classify as a bacterial case.

DR. A. A. THOMMEN, NEW YORK CITY.—I should like to ask Dr. Bullen in what portion of the 79 per cent who gave positive skin reactions, the reactions were of undoubted significance, excluding of course the hay fever subjects.

PRESIDENT CLARKE.—My feeling is that if one goes into the history more carefully of a great many of these people who date the onset of their asthma to operative interference, it will appear that the asthmatic symptoms would have occurred whether or not an operation was done.

In my experience, the diagnosis of hay fever has seldom been made until after the second or third season of symptoms.

DR. BULLEN.—I am sure we are all agreed that there are two definite indications for tonsillectomy: one, nasal obstruction, and the other, infection of the tonsils. But I should be greatly edified if someone would tell me when tonsils are infected. My nose and throat friends assure me they do not know.

Answering the skin reaction question, I should say offhand it would be high. As to the optimum time for tonsillectomy, I am not sure.

Studies in Asthma: XII. The Plant Pollens of New England. Their Relative Importance. A Preliminary Survey. F. M. RACKEMANN, M.D., AND LYMAN B. SMITH, PH.D., BOSTON. (For original article, see page 364.)

DISCUSSION

DR. JOHN MURPHY, PHILADELPHIA.—I should like to ask Dr. Rackemann whether a grass which I know by the name of "winter grass" is a factor in New England? Through the Pennsylvania districts we find that grass pollinates early and dies out after a wet spell. In August or September there is a separate crop.

DR. W. T. VAUGHAN, RICHMOND, VA.—The difference from year to year was interesting. I should like to ask Dr. Rackemann whether he has noticed any particular difference so far this year. This year we have found our trees pollinating at about the usual time and the grasses decidedly earlier; for instance, this year we found June grass pollinating by the middle of April. The same is true of some of the other grasses, which indeed are pollinating before some of the trees. Most of the trees were pollinating by the middle of April. The walnuts and the hickorys did not pollinate sufficiently to give rise to symptoms until the beginning of the third week in April. We have, however, in general a late spring this year.

In connection with Dr. Rackemann's third slide, we had an interesting experience last year with our ragweed curves. Durham has observed that ragweed pollinates earlier in the North than in the South, possibly because the season is shorter it has to get started earlier to get enough pollen distributed.

Dr. Rackemann's curve shows the onset of pollination before the tenth of August. In Richmond, we rarely find pollen on the slide before the eighteenth or twentieth of August and symptoms come very shortly after that.

Last year Virginia was pretty hard hit by the drought, and we had practically no ragweed whatsoever on our plates until the first day of September. There had been no rain until the twenty-seventh of August. We had one and eight-tenths inches of rain on the twenty-seventh, and four days later ragweed appeared on the slides. The next day patients began coming in with symptoms.

Thus there was a ten-day shortage as compared with the preceding three years during which I have been keeping the curves. In the first ten days of September, there was an overproduction, enough to balance the preliminary deficit as compared with the preceding three years.

After that we had a heavy average pollen concentration, terminating at the usual time. So, I am asking Dr. Rackemann whether he noticed any drought ef-

fects last year. We had a very definite drought effect with a ten days' delay and then a good heavy average concentration. The onset and severity of clinical symptoms corresponded.

DR. A. F. COCA, NEW YORK CITY.—The day in Boston is longer than it is in Richmond. The temperature is not sufficiently lower. This might explain the appearance of the pollen earlier in Boston.

DR. A. VANDER VEER, JR, NEW YORK CITY.—I think we still believe that the grasses biologically are so closely allied, an extract of one grass will protect against them all.

For the last six or eight years, we have used timothy extract alone for all our grass cases. With reference to the two charts, we find that year after year we get at least 1 to 3 per cent better results in our grass cases than in our ragweed. Occasionally we check timothy grass against Bermuda and other grasses, and each time that we have done this we have found the results of the tests were identical, and therefore, we concluded an extract of the timothy grass would protect against Bermuda grass pollen. We have had patients who have gone South, where they are exposed to Bermuda grass and not to timothy, who do as well with the timothy grass extract as they do here in the North, and conversely. Dr. Chobot treated several patients here in New York with an extract of Bermuda grass pollen and they did as well as the previous year when treated with an extract of timothy pollen.

We were fortunate enough to have a pure plantain case come to us a great many years ago. We treated that case for two or three years with grass pollen extract (as we did not know about plantain then). Of course his hay fever was not improved but we secured a good record of his clinical trouble. We found that it began before the fifteenth of May and he had his maximum trouble the first two weeks in June, which cleared up rapidly after the middle of June. While he had an occasional attack through July, it was very mild.

When he was treated with plantain extract, his symptoms cleared up, and the last four or five years he has had little hay fever.

We also checked back and found persons not doing well the last two weeks of May and the first two weeks of June react to plantain as well as grass pollen, and in these cases we combine plantain and timothy extracts. Conversely, if the symptoms do not begin until the twenty-ninth or thirtieth of May, it almost surely is not a plantain case but a pure grass case.

DR. LESLIE N. GAY, BALTIMORE.—During the past two years we have carried on a pollen survey of the city of Baltimore in conjunction with the Botanical Department of the Johns Hopkins University. Our results have paralleled somewhat the preliminary survey of Dr. Rackemann.

There is one striking exception. We have found that timothy grass is of minor importance. In the first place this plant is a cultivated grass. Orchard grass on the other hand grows in much the same manner as a weed. It can be found during the months of May and June on any vacant lot and along all of our roadways. The pollen of orchard grass is most abundant in comparison with the small number of pollen grains of timothy grass.

It is of interest to note that a number of Baltimore men have used timothy pollen extract in the treatment of individuals sensitive to this grass and the results have been most satisfactory. This suggests that in all probability treatment with timothy protects the individual against other related grasses.

DR. A. H. W. CAULFEILD, TORONTO.—In the pollen season, one thing has come out strikingly and that is that a weed or grass may be prevalent one year, will seem to be overgrown, and then not appear to any relatively great extent the next

year. It depends upon the atmospheric conditions. There is a variation of at least two weeks in the annual appearance of pollen in many of the more important plants.

I think there is a great deal of difference whether one treats with the extract of one grass or another and I believe that better results are obtained with more than one pollen solution.

DR. RACKEMANN.—There is one thing I should like to emphasize about this chart. The first of it was made up from specimens in the herbarium at Harvard, all of which are labeled with dates, which could be tabulated without difficulty. The first part of the season, therefore, down to the middle of June represents the extremes of pollen production. From June 15 on, the observations are field observations. This winter we have gone back to the herbarium again and find in most cases that the field observations made later in the season do fall into line with the herbarium.

Evidently, variations in the time of pollen production are much more marked in May and June than they are later. Ragweed seems to appear at the same date from year to year.

If I may have one minute, I would like to show you Dr. Cooke's chart which I happen to have. This chart was made in 1926 and shows the seasons very much shorter and more like the elm chart which I showed.

A question was asked about winter grass (*pao summa*). In the herbarium there were specimens back to early April and other specimens showing pollen in September. Dr. Smith believes it gives off pollen at all seasons, even in winter after the time of frost.

Local Passive Transfer to a Frequently Recovered Strain of Staphylococcus Hemolyticus. Case Report.

A. H. W. CAULFEILD, TORONTO.

(For original article, see page 372.)

DISCUSSION

DR. EARL BURKY, BALTIMORE.—If one mixes the toxin that was introduced with an antitoxin obtained from a rabbit, it may be one way of introducing enough antitoxin to prohibit definitely the skin reaction.

DR. LEO H. CRIEP, PITTSBURGH.—Without attempting to go into any lengthy discussion, I should like to discuss a case of undulant fever. The patient had been ill three or four months. He gave a positive agglutination test of 1 to 280. When tested with one strain, he gave a definitely positive skin reaction, a negative reaction to the control. We have obtained one emulsion of bacteria from the University, the other from Dr. Levine of the State Department of Health in Oregon. We got a positive passive transfer in two out of three of these substitutes.

DR. CAULFEILD.—In reply to Dr. Burky, I appreciate the fact we might mix our toxin and antitoxin. Personally, I thought it would be preferable to try it as I did. There has not been as much work done on this extraordinary case as I should like to do, but the patient objects strenuously to everything that is done. That has to be taken into consideration.

At least fifteen or twenty people have been tested, not with the toxin but with the emulsion. Those two receptors were tested at the time the reinjection was made and there was absolutely no reaction.

In regard to the media, it was isolated on blood agar on which we made our initial culture. The media used for the preparation of toxin is a synthetic broth such as they use at the Connaught laboratories in the preparation of their toxins. It should not carry any substance to which one is liable to be sensitive.

Vernal Conjunctivitis. L. LEHRFELD, M.D., PHILADELPHIA. (For original article, see page 328.)

DISCUSSION

PRESIDENT CLARKE.—These cases were tested at our Asthma Clinic and they gave positive reactions to the pollens, but in no case did we find the reactions that we see in the ordinary case of hay fever. The reactions were positive, and usually picked out one pollen in preference to the other pollens so that it was not a generalized reaction to all pollens. We had to use a point one solution to get the reaction.

It is hard to see from the history how these patients could get their whole symptoms from the pollen, but beyond any question these patients do have positive skin reactions to the pollens.

DR. A. VANDER VEER, JR., NEW YORK CITY.—Very few of the cases of vernal catarrh we tested gave skin reactions. It is difficult to assign all their symptoms to the pollen as some of our cases started as early as February or March and their symptoms would appear at any time when the weather became warm.

DR. BURKY, BALTIMORE.—We have studied a fairly large series of chronic conjunctivitis as well as vernal conjunctivitis. In most of these cases we have been finding anaerobic organisms. The ones most commonly found are *Staphylococcus parvulus* and an organism which resembles the acne bacillus very closely. We have never found these organisms in normal conjunctivae. Whether they are of any significance we are not prepared to say at this time.

DR. T. D. CUNNINGHAM, DENVER.—I have had one patient under treatment for five years. She was negative to foods and pollens. In an attempt to cure her, I obtained a vaccine. She has obtained definite relief from the vaccine. The organism may vary from year to year with her. I have tried to discourage her from coming in but she says she must come in; if she does not take the vaccine she is much worse. Her symptoms start in February, before there is any pollen in the air and will persist long into the summer. For five years, she has come in of her own volition in February for a repetition of the vaccine treatment.

DR. RICHARD A. KERN, PHILADELPHIA.—I should like to mention a case. A young man had typical vernal conjunctivitis and an eczema that had lasted since childhood. On testing, we found he was sensitive to horse dander, grass pollen and certain foods. Treatments with horse dander and grass pollen extracts gave only temporary relief. An avoidance of certain foods has resulted in a complete relief of both vernal conjunctivitis and eczema, for four years.

DR. A. A. THOMMEN, NEW YORK CITY.—I should like to ask just how successful radium is in relieving the symptoms. I should like to remark that six years ago I investigated a series of such cases. As is well known there is a definite relationship between the intensity of symptoms and the particular time of the year. I remember at that time in February, we had a snowfall followed by a spell of warm weather. There was not any deciduous vegetation to be found in the vicinity of New York, and yet, several of these patients suffered definitely with the symptoms of vernal conjunctivitis at that time because it was unusually warm and sunny. I investigated the number of spores found in the air at that particular time of the year but could come to no definite conclusions.

DR. JOSEPH HARKAVY, NEW YORK CITY.—I wonder if the matter of physical allergy has been taken into consideration in these cases.

DR. LEHRFELD.—In reference to the case of conjunctivitis observed in February, I remarked in this paper that the slightest approach of warm weather in the winter will bring on an attack of itching. This may be explained by the fact that the follicles are so large that the organisms are caught and the patient becomes sensitive to bacteria. Heat may precipitate an attack of itching.

In answer to Dr. Harkavy's question, as far as passive transfer is concerned, it was not tried.

We undertook the treatment of fifteen cases during the past two years. It was supervised by one of our experts at the hospital. We have come to the conclusion that radium will give some relief from the itching. It will reduce the pathological lesions. The effective use of radium in one case of vernal conjunctivitis does not mean it will cure the disease any more than radium applied to the nose will cure hay fever.

It was remarked that vernal conjunctivitis does last longer than the distribution period of pollen, and that is true for the reason that patients become subject to vegetated bacteria. The patients do not show any serious involvement of the nose or throat; most of them are children or adults in pretty good health.

Vaccinial Encephalomyelitis. HARRY H. DONNALLY, M.D., WASHINGTON, D. C. (Abstract.)

Five children had postvaccinial encephalitis.

Their cases may be summarized thus:

They were all primary vaccinations; there were four boys and one girl; four were six years old, one seven years; they all occurred in October, 1930, from vaccinations prior to entering school. In all, the vaccinations had not healed.

In three, the most severe manifestations coincided with or closely followed the peak of the take, in the two other children serious symptoms occurred in the fourth week after inoculation.

Onset: In the three with early onset and symptoms of the most diffuse lesions in the brain and spinal cord, the onset was gradual; in the two with late development of symptoms which seemed due to less diffuse lesions, the onset was abrupt and stormy, occurring in the fourth week after inoculation. In two cases, symptoms manifested themselves early and insidiously, and increased rapidly to definite paralysis, about the peak of the vaccination sore. One child had headache for two days beginning on the tenth day, then vomiting, and by the fourteenth day symptoms suggesting acute tetanus. Two of the children had trismus.

Lesions: All five presented symptoms of more or less severe, diffuse encephalomyelitis. Two of the five cases showed slight spinal fluid changes; three had normal spinal fluids.

Fever: Three children had fever, 101° to 104° for a few days. Two others had no fever.

Urine was essentially normal except for cystitis in the catheterized girl.

Leucocyte counts made in two cases, were as follows:

13,200 with 80 per cent polys.
11,300 with 81 per cent polys.

Recovery: All five cases rapidly and completely recovered, and were found six months after the onset of their encephalomyelitis to have no residua of brain or spinal cord damage.

DISCUSSION

DR. F. M. RACKEMANN, BOSTON.—I should like to know what the incidence of this condition is in normal vaccination, and also if in these cases there was evidence of any allergy in the victims.

DR. S. S. LEOPOLD, PHILADELPHIA.—It seems rather remarkable, if I understood the speaker correctly, that only 600 cases were reported in a year and that five of them occurred within a period of a few weeks at a single source, three of them occurring in the experience of one man and two cases among his colleagues. I wonder, therefore, whether any effort has been made to trace the source of vaccine, or whether there is any evidence that the three cases in the essayist's personal experience may have had the same source of vaccine used. It seems to me strange that one man should have had the bad fortune to encounter this thing five times in one month.

DR. GEORGE FLAMM, BROOKLYN.—I should like to know whether any organism was cultured from the blood or spinal fluid of these cases.

DR. DONNALLY.—The National Institute of Health, as I said in my paper, has collected beginning with the first three cases reported from Prague in 1924, a little over six hundred cases. Fifty-one have been reported from the United States, up to the end of 1930. As I said in my paper, doubtless many cases remain unreported.

I agree with Dr. Leopold, if this disease is so uncommon, how could it happen that I saw five cases last October? I believe it is a thing that is going to come to the fore more and more. Possibly it has been diagnosed as something else—acute tetanus is one of the things, poliomyelitis, or lethargic encephalitis.

In regard to Dr. Rackemann's question, as to the number of cases among those vaccinated, the incidence so far reported is exceedingly low. It is estimated that there were about five thousand school children vaccinated in Washington in September and October, 1930. Most of these cases were vaccinated in the latter part of September, just as the schools were opened, so that they could get in. There were these five cases which came to the Children's Hospital, and possibly one or two others that I have heard of. That would make the incidence about one in a thousand.

Dr. Armstrong, who addressed this Society on one occasion, has been assigned to the study of vaccination, and he estimates that there was one case of encephalomyelitis to about three hundred and fifty thousand vaccine points sold by the manufacturers.

These cases were admitted with the disease. I know nothing about any allergic relationship in them. One theory holds that the disease may be an allergic manifestation.

The frequency of it among vaccinated persons is very low but it may be greater than the figures would indicate.

There have been commissions in England and in Holland, particularly, investigating this subject for years, and these reports are available. Nothing can be incriminated in the vaccine lymph used. That has been thoroughly worked

out in England, Holland and this country. In every one of these cases that I have reported, the vaccinator, the lymph used, and so on, were investigated by the local health department and the National Institute of Health in Washington. Most of the five thousand vaccinations done in Washington were done with the lymph from one manufacturer and the incidence of encephalomyelitis was exceedingly low. The Institute of Health followed this lymph into various parts of the country and it could not be incriminated.

Several spinal fluids were inoculated into guinea pigs with negative results; they were all cultured, and no organism was found either on smears or cultures from the spinal fluid.

The cause of the disease is not known. There are interesting theories, but so far they are theories. Dr. Simon Fletcher, in an article in the *Journal of the American Medical Association* of February, 1930, discussed them at length. As they are all theories and no conclusions are drawn, I did not have time to present them to the Society.

Studies in Contact Dermatitis. I. The Nature and Etiology of Pollen Dermatitis. AARON BROWN, M.D., E. L. MILFORD, M.D., AND A. F. COCA, M.D., NEW YORK CITY. (For original article, see page 301.)

DISCUSSION

DR. A. H. W. CAULFEILD, TORONTO.—Might I ask if Dr. Brown has come to a conclusion as to how to treat this dermatitis?

DR. HUBER.—I have found that 4 per cent of my patients give a definitely positive skin reaction to the anhydrous ether extract of pollens. I have not made nitrogen tests of this pollen fat. No one of these patients had a dermatitis. I have recently seen a physician planning to do surgical work, who was so sensitive to rubber that he could not wear rubber gloves without leaving a severe dermatitis. The causative agent in this case was found to be a chemical used in the preparation of the rubber. The rubber companies are now studying the chemicals that cause dermatitis in their employees.

DR. A. BROWN.—There are just three points we want to stress to clarify the difference between inherited human hypersensitiveness and contact dermatitis:

(1) Pollen dermatitis is as prevalent among nonatopic as among atopic persons.

(2) Pollen oil dermatitis is in the class of poison ivy dermatitis.

(3) The treatment of pollen oil dermatitis is by the use of the oil and not by the pollen antigen.

The cases cited came at the end of the season. We are interested in studying them but had no time to treat them that year. This will be done in 1931, with pollen oil.

Transfer of Skin-Sensitizing Antibodies. SAMUEL D. BELL, M.D., NEW YORK. (Abstract.)

This paper deals with ten mothers, five of whom suffered from hay fever and five from asthma.

Direct tests were done on these mothers and their ability to transfer this reaction while carrying their children was shown in the skin of two nonrelatives.

When a positive transfer was obtained, their serum was then diluted

to a point where it could no longer show this transfer. Evidence of positive transfer was shown in most cases in a dilution of 1 to 40 and in one case in a dilution of 1 to 320.

Cord blood was obtained at birth and blood from the child at varying periods from a few hours to several days after birth, but neither of these would give a passive transfer even when undiluted, the sites being retested with the same material and strength to which the mother reacted and then with stronger material when possible.

DISCUSSION

DR. A. F. COCA, NEW YORK.—Dr. Bell has spoken to me about this work. It reflects, it seems to me, the difference that we know so well between the immune antibodies and the reagins. It has been known for a long time since the classic experiments of Ehrlich upon the passing of ricin antitoxin from the mother mouse to the offspring, that the ordinary antibodies reach the fetus from the mother through the placenta. Later there were other papers on the transfer through the placenta, and also through the milk, of immune antibodies. In explaining why the reagins do not get into the child, I would recall the rapid and permanent fixation of the reagins to the tissues of the skin in the Prausnitz-Küstner experiment. The reagins have a strong affinity for tissue which differentiates them from the normal or the ordinary immune antibodies. Freund in Philadelphia has shown that immune antibodies are soon distributed through the body after subcutaneous injection, but the reagins attach themselves to every tissue they come in contact with; hence we can easily see why they could not pass through the placenta, since the mother's blood does not mix directly with the fetal blood.

DR. WALZER, BROOKLYN.—Dr. Bell's work is in line with something we have been trying to do for the last two or three years at the Jewish Hospital of Brooklyn. I ran a few experiments with Dr. Kornfeld and Dr. Weber of the Department of Obstetrics, and we tried to prove several things with the method of passive local sensitization.

I am glad to be able to confirm Dr. Bell's findings in regard to the failure of reagins to pass through the maternal placenta which we noted in 3 or 4 cases of mothers with hay fever. We attempted to do several other things along the same line. We tried deliberately to sensitize the offspring by having the mothers eat excessively of certain foods, particularly substances which we knew were very easily absorbed into their circulation from the gastrointestinal tract; substances such as nuts and eggs. Of course, in the half dozen cases or so where this was tried, we could not succeed in demonstrating any sensitivity in the newborn.

We attempted to check up the idea that has been occasionally expressed that infants are sometimes born sensitive. Balyeat reported a positive cutaneous reaction to wheat at birth, but he failed to test the blood for reagins. We tested 100 newborn infants routinely with milk, eggs and wheat. Skin testing on the newborn is a very difficult thing to do. We were surprised to see how many positive reactions we obtained with everything with which we tested. This was particularly so as far as the scratch method was concerned. The slightest touch of the needle caused bleeding and erythema. We found the intracutaneous method of testing more satisfactory in that it seemed, if done properly, to cause less trauma. In 100 cases, although at times some reactions *seemed* to appear positive, repetition of the test or further investigation failed to prove these reactions to be specifically positive.

I believe that we ought to be cautious in accepting the assumption that children are born sensitive. The reason for this is obvious if our work on unaltered

protein absorption is kept in mind. We tried feeding the egg white antigen to newborn infants who had been passively locally sensitized, and found that a positive reaction developed before they had finished their bottles. The gastrointestinal tract of the newborn infant is almost like a sieve. If the idea of antigenic stimulation is needed to explain the development of sensitivity, and if the work of Donnally is accepted that unaltered protein passes through the mother's milk, there is sufficient antigen entering the infant's circulation after birth to explain adequately any sensitivity which develops within a month or two, without recourse to the theory of intrauterine sensitization.

I think Dr. Bell is to be congratulated upon a wonderful piece of work.

DR. BELL.—I was not able to show the chart which gives the dilutions of the tests done. The fact remains that there was a striking difference between the cord and baby's blood and that of the mother. The cord and baby's blood were tested on the same people who had shown a passive transfer from the mother's serum in dilutions; we were not able to demonstrate any reaction with the undiluted cord and child's blood. The inability of the cord and child's blood to sensitize those same people was very striking.

Blood Pressure in Allergic Individuals. JAMES MCLAUGHLIN, PHILADELPHIA. (For original article, see page 360.)

DISCUSSION

DR. WALZER, BROOKLYN.—I should like to ask the speaker whether he can give us some information as to what is the natural reaction in regard to blood pressure in an attack. That is one of the most disputed points in the literature. Some tell us an attack raises the blood pressure.

Dr. Alexander in his report, after very careful attention to this point, tells us there is a fall of blood pressure during the attack, that is, without the administration of adrenalin. I wonder whether the speaker or anybody present could report upon his experience with blood pressure in asthma.

DR. MCLAUGHLIN, PHILADELPHIA.—We did not make any special studies on the blood pressures during an attack. The only thing I can state is from Dr. Alexander's work wherein he showed the enormous increase in the venous pressure during an attack which causes a fall in the arterial pressure. This was attributed to the great increase in the intrathoracic pressure which is quite evident during an attack.

Incidence of Diabetes Mellitus in Asthmatic Patients. N. SWERN, PHILADELPHIA. (For original article, see page 375.)

DISCUSSION

DR. LOUIS TUFT, PHILADELPHIA.—I wonder whether Dr. Swern made any estimations of the acid-base balance and whether he has any knowledge of the effect of acidosis on asthmatic symptoms. I mention that because I believe it was Beckman who made the statement that a combination of diabetes and allergy is rare and that diabetes and epilepsy is rare, and mentioned these in support of his contention that there is in allergy a disturbance of acid-base equilibrium. In diabetes, there is a tendency toward acidosis and in epilepsy a high fat diet leading to acidosis tends to improve the conditions.

DR. A. H. FINEMAN, NEW YORK CITY.—We saw a few cases of allergy associated with diabetes. I found one child, twelve years of age, who had severe

hay fever. She received pollen treatment and did well on it, but the diabetes has been going on just the same. She is on a strict diet with a considerable amount of insulin. The others were adults who had diabetes and asthma.

DR. LEO CRIEP, PITTSBURGH.—Along the lines suggested by Dr. Tuft, Dr. Beckman spoke at the last meeting of the Association about the possibility of alkalosis being a factor in allergy. In a series of fifty patients I am about to report, as an additional study, we carried on tests of carbon dioxide combining power of plasma and our findings were universally normal. Neither by that method nor by the P_H ion concentration of blood, could we show definite changes from the normal.

DR. GRAFTON TYLER BROWN, WASHINGTON.—I want to corroborate what has just been said with respect to the blood sugar and CO_2 combining power being almost invariably within normal limits in asthmatic patients. With reference to Dr. Beckman's contention that in allergic individuals the tendency is toward alkalosis, I should say that although determinations of the carbon dioxide combining power in allergic patients of mine have all been within normal limits, they have tended toward the low level or acid side. Also, blood-sugar determinations on my allergic patients have all been within normal limits, and have tended to be low normal rather than high.

DR. S. S. BULLEN, ROCHESTER.—Dr. W. S. McCann has made a suggestion. He states that in the normal individual insulin and adrenalin seem to oppose each other and it would be natural to suppose in the diabetic, where the insulin is low, the adrenalin might be relatively high and that might be an explanation why an individual who has diabetes might not have manifestations of allergy.

DR. HUBER.—In the past year I have had two patients who had been treated for pollen disease develop diabetes, one an old lady of seventy years and one a girl of twelve years. This is the first time I had seen both diabetes and pollinosis in any patient.

PRESIDENT CLARKE.—I do not think the fact that these diseases do not occur in the same individual will throw light on the acid-base or adrenalin-insulin reaction. This one individual was one of the most severe pollen asthmatics we have seen for a long time. She was tickled to death with the result of her treatment. She was only in bed two weeks with asthma; heretofore, she was laid up for six weeks with the asthma.

At the same time that Dr. Swern took the blood, the patient was tested in both skin and eye and gave strongly positive reactions to our tests. We had the two mechanisms, the diabetes and the asthma, active in the same patient within the space of the same hour.

Is there any further discussion? Dr. Swern, will you close?

DR. SWERN.—We have not done any acid-base determinations on any of these patients. As far as the effect of acidosis on these individuals is concerned, I have not seen any diabetic asthmatics having acidosis.

With reference to adrenalin-insulin, possibly it is the exception that proves the rule. We had one, who since died of diabetes, who was taking insulin and had symptoms of acidosis, and symptoms in her chest.

As Dr. Clarke just explained, we had one patient who was sensitive to pollen and still had a high blood sugar.

Department of Reviews and Abstracts

Selected Abstracts

Allergy in the Middle and the Internal Ear. Proetz, A. W.: Ann. Otol., Rhin. & Laryng. **40**: 67, 1931.

Allergic disease of the ear may simulate other diseases of the ear and is often difficult to recognize. It is suggested that differentiation may be made by the nature of the onset which may often be accompanied by allergic disturbances in other parts of the body, and by a careful examination for any possible allergic history in the patient or his immediate family.

A case report is given in considerable detail of a patient suffering from reactions in the labyrinth of the ear. The patient when first seen complained of intermittent tinnitus and vertigo for the preceding five years. He had suffered a severe attack four weeks previously, with protracted vomiting and vertigo. The physical examination was essentially negative. Attacks continued at intervals of several weeks. A tooth showing signs of infection was extracted and the patient put on a diet of buttermilk and Bulgarian bacillus. An increase of symptoms followed. About a year later, a nose and throat examination which was otherwise negative, showed a patch of edema in the nasopharynx, suggesting the presence of allergy. The patient was found to be sensitive to milk, butter and cheese. Removal of these articles from the diet was followed by an almost complete subsidence of symptoms. Further attacks occurred only upon the ingestion, deliberate or accidental, of these foods.

A second case report is given of an edema of the tympanum accompanied by severe pain resulting from the ingestion of a foreign protein to which the patient was sensitive. This is a condition more prevalent than is generally realized.

The patient, aged fifteen months, was first seen in consultation with a pediatrician who had opened the ear seven times during the current attack. The membrana tympani was a bloody mass, and there was some pus in the canal. The patient was in an attack of asthma at the time, and it was believed by the pediatrician that the ear infection precipitated the asthmatic attack. At a subsequent date, during an-

other attack it was observed that the earache did not precede the asthma but was coincident with it or followed it. The drum membrane was not incised and the otitis media subsided with the asthmatic attack. The child was found to be sensitive to egg, potato, chicken feathers, cotton seed and horse dander and in lesser degree to wheat, goose feathers, duck feathers and cat hair. Upon elimination of these contacts the asthma improved to a marked degree and there was no recurrence of the ear symptoms.

A Physical Method for the Treatment of Bronchial Asthma. Wellisch, E.: Med. Klin. **27**: 244, 1931.

A method of treatment is described in which is combined diathermy and radiation from a quartz lamp. Diathermy of the lungs takes place daily, or at the least every other day, while radiation is employed once or twice a week. The duration of the cure advised is six to eight weeks. Diathermy may be taken by the patient either in a sitting or in a reclining position. Treatment at first continues for ten minutes but is gradually raised in degrees of two minutes until a maximum duration of twenty minutes is reached.

The quartz light radiation is local and not general and has effect only when it produces an erythema. The dosage depends upon the individual skin sensitivity of the patient. According to the author, the principal factor in the curative effect of the quartz light erythema is a reflex action of the skin over the autonomic nervous system to the inner organs.

The method has been used on 22 patients with good results reported, only 4 remaining unimproved. Two case reports are appended.

Contribution to the Treatment of So-called "True Asthma." Dudan, A.: Schweiz. med. Wchnschr. **61**: 137, 1931.

There has been much controversy over the queston of the etiology of "true asthma." There is one hypothesis that one finds constantly recurring; the relationship between tuberculous infection and asthma. The author recognizes an apparent incompatibility between tuberculosis and asthma, finding them rarely associated but suggests an explanation other than incompatibility. His own recent work leads him to believe that in some asthmatics the tuberculous infection has assumed an attenuated, nonlesional character developing a power of chronic intoxication which reacts upon the neurovegetative system.

Experiments were carried out upon a number of patients. Treatment consisted of intravenous injections of Sanocrysine (which has a specific affinity for the tuberculous) in very fractionated doses beginning with 0.01 c.c. and mounting progressively to a maximum of 0.05 c.c. One injection a week was given at the beginning, then the injec-

tions were spaced gradually from ten to fifteen days, then one injection a month. The dosage, however, might vary with the individual. Good results were obtained; in some instances a complete relief from asthmatic crises being experienced. The number of patients so treated is preliminary to further study. Two case reports are given.

Clinical Treatment of Asthmatic Patients in Allergen-Proof Chambers. Storm van Leeuwen, W.: J. Lab. & Clin. Med. **16**: 442, 1931.

In a previous communication on the results with 80 patients treated in allergen-proof chambers, it was shown that 70 per cent were free from asthmatic symptoms after some days, 20 per cent were improved after two or three weeks and 10 per cent remained unaffected by the treatment.

The present results with 1,000 patients remain essentially the same but some additional observations were made. It is now possible to predict with some degree of certainty whether or not a given patient may benefit by residence in the chamber. A definite group that in all probability will not be benefited by this treatment, is the considerable number of persons who are sensitive to aspirin. Persons living in a moist climate usually give better results in the chamber than do persons who have been living in a dry climate.

The chief objects of admission of asthmatic patients to the allergen-proof chamber are:

1. *Observation*, enabling a correct diagnosis within a shorter space of time.

2. *Temporary improvement*, making possible judgment for the prognosis of the patient and his ability to work.

3. *Possibility of desensitizing*, the patient to allergens to which he reacts, especially in such cases where desensitization at home would be difficult or dangerous because of the variety and quantity of the contact in his environment.

The condition of the patient is measured not by the vital capacity but by the inspiration time (the time between the beginning of the deep inspiration and the end of the deep expiration) as measured by a spirometer on a kymograph.

Allergen-proof chambers have been installed in private houses and the results are reported to be generally satisfactory.

Some work is being done on treatment of tuberculous patients in the chamber. The indications are that the allergen-proof chamber permits the treatment of cases of tuberculosis in any place and in all climates with at least as good results as high altitudes would give in such cases.